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SYMPOSIUM: MINOR PSYCHIATRIC DISTURBANCES IN WAR AND CIVILIAN LIFE

THE DIAGNOSIS OF THE PSYCHONEUROSES*

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IN a discussion of the phenomena included in the term "psychoneuroses," it is essential to realize that the word does not apply to a specific disease but rather to the quality and degree of adjustment that a person makes to the problem of living. It relates to his satisfaction with life, the efficiency with which his abilities are mobilized and his effect on other people.

Although in certain cases there may be a constitutional predisposition to behave in a neurotic manner, it appears equally true that under fatigue, sufficient stress or a particular kind of stress, a normal person may for a time behave in a neurotic manner.

Before the actual experience with bombing in Britain, there was apprehension that civilians exposed to the intense and terrifying conditions created by air raids would react with panic, hysteria or neurosis. As a matter of fact, this has not happened. Under this kind of stress, pride or the fear of what other people might think is sufficient to maintain a freedom from neurotic manifestations. People become habituated to the threat of destruction very quickly and go about their affairs. There may be anger at the enemy, but that might well be classified as righteous indignation. Pathologic mental disturbance is extremely rare. Among people known to be neurotic, about 25 per cent have actually improved under war strain. This may be because the demands and opportunities for activity under the altered conditions are more vital than the issues creating the neuroses. Twenty-five per cent are made worse, and 50 per cent show little or no change. Children appear to be even less disturbed by air raids than adults. In general, there is a tendency for them to imitate adult behavior. It is interesting that the disorganization of a regular routine of life is more frequently a cause of neurotic behavior than the air raids per se.

In normal civilian life, some patients who seek help and are recognized as neurotic may be in trouble either because of a temporary conflict brought on by unusual environmental or personal difficulty that will pass or change with time, or because of a type of personality that has difficulty in adjusting to a normal environment most of the time. In the latter group, certain tendencies, which constitute a variation from what might be considered mature adult behavior, appear very often. A healthy-minded adult has acquired a capacity to observe his environment and appraise himself with some objectivity. With these data, action is initiated with respect for real limitations and without excessive optimism or pessimism about the results. He does the best he can and is willing to make mistakes and learn from them.

The neurotic has a strong subjective bias. He has intense wishes and fears. His behavior tends to be governed by attempts to protect his own feelings. He is prone to disregard facts that are inconsistent with his wishes, and to have difficulty in learning from experience. He may be puzzled, angry or hurt at the ineffectiveness of his efforts, but he continues to make the same mistakes. There is a strong tendency to assume that the trouble is with other people, or bad luck. One is reminded of the poor workman who blames his failure on the tools.

The neurotic does not consider himself realistically, as an object in a world of objects subject to natural law. He feels special, and eternally hopes

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that the world will adjust itself so that things will happen as he wishes, rather than as experience has proved. It is no comfort to him that natural law plays no favorites and pardons no mistakes. His orientation is egocentric, and there is a tendency to believe he is in some way a cause of all happenings, in any situation that includes him. If it is raining, his wish that it be a fine day had something to do with it. If people are unjust or cross, it is because they do not like him. It would not occur to him that they might be thoughtless, or might have indigestion. He interprets all phenomena in terms of their effect on his personal feelings and wishes, and has real difficulty in establishing an intellectual grasp of relations that transcend his subjective sensitiveness.

A second common finding is an inability to stand the tension of a delay between impulse and satisfaction. A plan of action that entails prolonged effort to achieve a goal tends to be interrupted—possibly by a phantasy of success, which replaces the need for further work. In imagination, the neurotic succeeds without discipline or the pain of failure or imperfection in accomplishment, and can always assume, "I really could have done it if I had tried." In situations of conflict that are slow to resolve, the neurotic frequently turns to some activity that assures quick satisfaction. Going shopping is a frequent palliative: one can see something that is desired, buy it, and feel a great sense of emotional relief. A woman in doubt whether she loves her husband ends up with a new hat, and the concern about the husband does not seem to matter. A boy should be studying for an examination, but finds himself reading a story in the *Saturday Evening Post* with the idea that it will relax his mind for study. By a shift to an impulse that permits immediate gratification, the tension of uncertainty and delay is evaded, and peace is restored in the nervous system. This solution obviously restricts the type of satisfaction that the neurotic may enjoy, and interferes with the development of potential capabilities through the discipline of training.

A third factor that neurotics appear to have in common is a hesitancy to act on their own independent opinions. They constantly appeal for advice or help. The comment is, "I don't know which way to turn," or "I don't know what to do." By insisting on being told what to do, they avoid the responsibility of errors in judgment, and establish the probability that by following direction they may at least win approval. Guidance is also taken as evidence of affection and support, in that it creates a kindly parental supervision. In conjunction with this lack of self-confidence, but less commonly expressed, is a quality of self-hatred: an unformulated sense of resentment for a self that fails to express its wants and to dare as an independent entity to further their realization in the world of reality. Self-love is important in creating the assurance essential to independent function, and the neurotic never seems sufficiently sure of his own value. Being insecure in his own sense of value, he is abnormally concerned about whether he is loved and accepted by the people about him, and tends to measure this by the degree of their approval. It is as though other people were significant only as they existed to praise or blame. Because neurotics fail in becoming independent persons, they are incapable of stimulating real love or friendliness in a mature sense, and tend to be pitied, tolerated or dominated. Because of their unformulated distrust and hate of themselves, they are prone to become suspicious and antisocial. They tend to be on the defensive and behave as though they expected other people to share the dislike and distrust that they really have for themselves. This may lead to a "sour-grapes" attitude, with retreat from social contacts, or a belligerent and stubborn aggressiveness. If they express an opinion, they feel obligated to enforce its acceptance, and have little or no willingness to discuss an issue or to tolerate the thought that their opinion may be in error. To "give in" is considered a personal failure, so that they have an enormous need to be right about everything. Aggressiveness deteriorates into temper and hurt feelings. These patients are constantly in trouble in situations demanding emotional maturity. They do not establish either healthy independence or dependence.

Another neurotic difficulty is an inability consciously to inhibit one wish that another, more appropriate at the moment, may have an opportunity for fulfillment. It is as though, once a wish had registered, it compulsively held the field to the exclusion of all other possibilities. They want what they want when they want it. Substitutes have no rating as any satisfaction. If one tied a string to a piece of meat, and just as the neurotic started to swallow, one pulled it out, to run true to form no further enjoyment in swallowing would be possible. The neurotic wish would insist that the frustrated swallow be completed. Nothing but this would be satisfying. The impossibility of fulfilling this hope would be no deterrent to its perpetuation, and the acceptance of the reality of pleasure in another swallow would be rejected as an evidence of failure. Continued consciousness of such frustration would occasion too much mental suffering, and the mind appears to have some automatic function by which a conflict of this type

may disappear from consciousness without final resolution in acceptance of disappointment or defeat. The wishes that have disappeared in this way, however, leave some alteration in the neural mechanism by which there remain internal foci abnormally susceptible to reactivation by appropriate stimuli. Such a residuum constitutes a threat that the mind may at any time be under the necessity of dealing with unfinished business; it is not free to devote its full potential to the resolution of present-day conflict. There is difficulty in thinking in terms of what is the lesser of evils. The neurotic, having been spared the pain of frustration by defense mechanisms that avoid the acceptance of disappointment, is at a disadvantage in utilizing conscious choice in dealing with the complex problem of living in a world that is normally full of frustration.

Another finding is the rarity with which a neurotic achieves a normal sexual adjustment. There may be retention of infantile forms of expression, frigidity, impotence, premature ejaculation or difficulty in co-ordinating tenderness and affection with the physical function of sexuality.

Any or all of these disturbances of personality and adaptation may be subordinated to a presenting symptom suggesting organic disease. Pain, weakness, gastrointestinal or cardiorespiratory symptoms, insomnia and over-reaction to illness, to mention but a few, may be the overt reason the patient seeks medical help. Sometimes, the symptom is quite independent of any pathologic lesion. In other cases, continued anxiety, by altering sympathetic innervation, produces functional disturbance, most commonly in the gastrointestinal and cardiovascular systems. In this way, symptoms may be the direct result of physiologic changes in organs but the indirect result of disturbance in the patient's emotional life.

If one allowed a dog to bark at a cat, removed the dog and brought in an observer, there would be obvious physical changes in the cat. A rapid pulse, hair standing on end and dilated pupils might suggest a hyperthyroid disturbance; x-ray study of the intestine might show abnormal peristalsis; and examination of the throat might reveal hyperemia with the possibility of some undetermined infection. In spite of the accuracy of the findings, they would not show what was fundamentally wrong with the cat. Therapy devised to correct any of the symptoms would fall short of dealing with the total situation.

Everyone is constantly reacting to a very complex environment, with plenty of "barking dogs." Behavior depends on constitutional factors, some of which may be hereditary, the character of the family in which he grew up, education, contemporary social ideals, and the nature and intensity of the stresses to which he is exposed. Studies are now in progress to determine more of the physiology of emotion, but therapy to a great extent must be directed toward understanding and influencing the psychologic factors involved.

In differential diagnosis, one must consider such organic conditions as brain tumor, cerebral arteriosclerosis, hyperthyroidism, anemia, diabetes and drug intoxication, all of which may have symptoms suggesting a neurosis. Two other mental conditions may be mistaken as psychoneurotic. In patients suffering with a manic-depressive psychosis, one may be given a cue from the marked loss of weight that frequently characterizes this disease; and there is more obvious slowing of thought and inability to concentrate. Self-condemnation is more outspoken, and with less justification. There is often the comment that the mind is in a kind of fog that may lift at times for no reason at all. The depression frequently varies during the course of the day, without apparent cause. In the early manifestations of dementia praecox, the most characteristic feature is apathy. There may be suggestive ideas of reference, obvious overevaluation of indifferent environmental conditions, a paranoid trend in commenting on personal relations and, often, frank hallucinations, if one looks for them.

The diagnosis, "psychoneurotic state," should not be made merely on the basis of exclusion of organic disease as a cause of symptoms. It is not the result of imagination, and the one most futile comment to the patient is the advice to forget it.. Psychoneurotic symptoms are the result of a definite disturbance in the patient's emotional life. He is faced with some adaptation that is too difficult, and an attempt should be made to help him understand the nature of his problem, and to find an effective solution.

It should be remembered that the tendencies chosen to illustrate some of the neurotic's personality problems gain emphasis by isolation and do not present a true picture of the total individual. As a group, they have more than average intelligence, can be helped and are grateful for it. The neurotic is his own worst enemy and needs help to get out of his own way.

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PSYCHIATRIC COMPONENTS IN MEDICAL DISEASE: PSYCHOSOMATIC MEDICINE*

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DURING the last two decades, a new field has opened for the investigation of certain medical illnesses in which psychiatrists have shown interest. This field, often referred to as psychosomatic medicine, deals primarily with medical and surgical diseases that are properly within the province of internists, surgeons and medical specialists. The illnesses studied are those in which there exists a pathologic lesion, in contrast to the psychoneuroses, — especially hypochondriasis, — in which no known pathology exists. The etiology of these illnesses is as a rule unknown. Repeated observations have demonstrated that stresses and strains arising from the environmental situation and from difficulties in the personality of the patient play a significant role in the precipitation and in exacerbations of these illnesses. From studies in the neuroses and psychoses, psychiatrists have become familiar with the significance to the patient of specific situations and with the intricacies of personality function. This information has been applied to psychosomatic medicine in the hope of throwing light on the puzzles presented to the physician by these illnesses. The systematic approach to these special problems is still in its preliminary stage, and not more than the surface has been scratched. Yet sufficient work has already been done to indicate the validity of this approach. This paper reviews briefly the most striking studies that have appeared in this field.

It has been found that certain organ systems seem to be more readily involved than others. These systems are essentially those whose activities are actuated by the autonomic nervous system. One is apparently dealing with episodic reactions, which in many cases result in irreversible pathologic processes. The typical feature of these illnesses is that they are of long duration and characterized by exacerbations and remissions; they strongly resist treatment. Certain factors, especially allergic factors, play a role in the development of some of these disorders and yet do not alone explain the exacerbations and remissions. Of the many and confusing interrelations presented by the study of these illnesses, the best established seems to be a temporal relation between exacerbations and events or situations confronting the patient. In a few illnesses, a relation between the clinical diagnosis and the personality of the patient seems established from several sources. The role that situations and personality factors play in the etiology of the illness is least well established.

Studies that have been undertaken have made use of three methods of approach. Most of the studies concerned with establishing correlations depend on the history obtained from the patient or from some other source, by means of interviews or questionnaires. Even though large numbers of patients can be studied in this way, the limitations and sources of error are obvious. One would have to have access to data dealing with every single exacerbation and remission of the illness, a task hardly possible by the history method. The dependence on the memory of the patient and the avoidance of suggestion on the part of the interviewer represent the major difficulties. In dealing with the personality traits of patients, one is faced by the added difficulty of using descriptive words, about which there is little agreement among investigators.

Another approach concerns itself with the careful and intensive study of small groups of patients, either by intensive psychiatric study or by rigid psychoanalytic procedure. Here, too, correlations are drawn between situations and the exacerbation or remission of symptoms. In addition, attempts have been made to modify the patients by means of various psychotherapeutic approaches so that the same persons would no longer react pathologically to the presenting stimuli. There are also therapeutic reports and a few follow-up studies in some illnesses.

A third and most significant approach has been used in a very few studies. This is the experimental approach, which in these problems attempts first of all to find out what specific situations or ideas correlate with the symptoms. Attempts are then made to bring about exacerbations by carefully introducing discussions about these situations or ideas into the interview during a state of remission, avoiding as much as possible the introduction of other complicating variables.

The illnesses in which information is moderately complete are presented in some detail. The others are briefly mentioned. No attempt is made to

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include all the known facts. The literature has been comprehensively reviewed by Dunbar.[1]

Clinical Studies

Gastrointestinal Diseases

That patients react with their gastrointestinal symptoms to various types of situational and emotional stimuli has long been known.[2] Cannon[3] has clearly pointed out that states of worry and anxiety, grief, anger and other violent emotions can start a vicious circle leading through impaired digestion to mild inflammation and to impaired absorption, resulting in the vicious circle of emotional disturbances. Studies on patients with gastric ulcer, duodenal ulcer, esophageal spasm[4] and gastrospasm[5] have appeared in which the role of emotional factors has been considered. Recently, Mittelmann, Wolff and Scharf,[6] in a study of patients with gastritis, duodenitis and peptic ulcer, note that epigastric distress, nausea and even bleeding are precipitated or increased by emotional states. Anxiety, whether recognized by the patient or not, is an outstanding component of these emotional disturbances. In experimental work on patients with peptic ulcer, these authors report that such feelings as embarrassment, resentment, anger, anxiety and anxious anticipation are associated with a rise in gastric acidity and in total volume of secretion, with high or continuous peristaltic activity and hyperemia of the gastric mucosa. Feelings of security and relaxation are associated with low acidity and with less peristaltic activity. They postulate that the increased acidity, motility, hyperemia and even hemorrhage may have a bearing on the genesis of gastric and duodenal lesions found in the clinical picture of gastritis and duodenitis. The fact that mucosal erosions result from prolonged stimulation of the vagus[7] and also follow the intravenous[8] and intraventricular injection of acetyl-choline indicates that the parasympathetic outflow is most probably involved in the production of these lesions. It is not yet clear what factors determine the irreversible pathology that occurs in some cases.[9]

Psychosomatic studies on mucous colitis (mucous diarrhea), constipation, spasm of the colon and ulcerative colitis have been reported. Most of the work deals with mucous colitis, which was first well described by DaCosta.[10] Later authors emphasized the secretory and motor changes,[11] the inflammatory basis of the illness[12] and the role of food allergy.[13] White, Cobb and Jones,[14] in a broad study of mucous colitis, support the thesis that this disease is a physiologic disorder of the colon brought about by the action of the parasympathetic nervous system. The pathologic changes seen can be brought about experimentally by the use of cholinergic drugs,[15] although these changes have not been produced by the stimulation of the sacral outflow of the parasympathetic nervous system. In 92 per cent of the 56 psychogenic cases studied by White, Cobb and Jones, emotional tension was present, and the authors believe that this emotional tension was the commonest cause of the parasympathetic stimulation. In the more neurotic group of their patients, exacerbations of symptoms were associated with emotional tension in 56 per cent, whereas in the less neurotic group, a relation between tension and exacerbations of symptoms was found in 85 per cent. The higher correlation obtained for the less neurotic group was believed due to the fact that the emotional disturbances in this group were more frequently recognized, since "the sources of tension were always superficial and more readily understandable."

From a psychoanalytic study of a small number of patients, Alexander[16] reported three personality types associated with gastrointestinal symptoms. He considered that patients with primarily gastric symptoms had personality features characterized by activity, independence and efficiency. Of the patients with intestinal complaints, he distinguished a "colon type" with diarrhea as dependent persons who had marked tendencies toward giving, with feelings of obligation and guilt. He also differentiated a "constipation type," characterized by stinginess, dependence and need for accepting with no guilt and no need for giving. White, Cobb and Jones[14] confirmed the existence of these types among their patients. They were unable to corroborate fully the correlation postulated by Alexander between the colon and constipation types and the presence of constipation or diarrhea. White, Cobb and Jones found that the emotion most characteristic of their patients was that of resentment. Patients with mucous colitis were also conscientious, rigid, meticulous people with compulsive tendencies. As a result of this rigidity of thinking and the tendency to dwell on disturbing topics, the tension was sustained over long periods. This protracted state of affairs is believed to result in the formation of symptoms.

In patients with ulcerative colitis, correlations between the exacerbations and special situations have been reported by Murray,[17] Sullivan[18] and Wittkower.[19] Lindemann[20] has most recently pointed out that these patients present a psychiatric disturbance characterized by apathy, a marked difficulty in communicating matters of emotional concern and a defect in "differentiating reality from subjective falsifications." Daniels[21] has em-

phasized in this group the need for dependence on some member of the family, usually the mother. Conflict develops in situations, such as engagement and marriage, that threaten this dependence. This conflict can be the precipitating factor.

Allergic Diseases

Investigations have been made on various diseases associated with specific allergens. Of these, the most work has been done on asthma[22] and on certain types of cutaneous disturbances, notably atopic dermatitis.[23] That the respiratory function can be influenced by emotions and situations has long been known. More recently, this question has been re-investigated, and it has been shown that, in anxiety states and hysteria, changes in rate of respiration, in total ventilation and in the pattern of respiration are associated with certain ideational and sensory stimuli.[24] Irregularities in respiratory rhythm are described in anxiety states,[25] and marked episodes of hyperventilation have been seen in hysteria.[26] These changes are all episodic and reversible.

Bronchial asthma. Many sporadic studies show that in acute attacks of asthma not only exacerbations of the condition but also, at times, remissions are associated with situations that provoke acute anger[27] or other violent affects. The demonstration of sensitivity on the part of patients to many allergens not only has removed the emphasis from the emotional factors for a time but also has made it difficult to exclude the possibility that every asthmatic attack is caused by an allergen unsuspected in the situation. Yet, in many cases, the presence of allergens to which the patient is sensitive does not alone explain the attack. Such factors as fatigue and emotional disturbances have been secondarily involved. More recently, evidence has been accumulating that asthmatic attacks can be brought on by hypnosis in asthmatic patients,[28] and even by direct suggestion[29]; the fact that several authors have used psychotherapy with good results when somatic therapy failed[30] has reopened the problem for systematic investigation.

McDermott and Cobb[31] found that in a two-hour interview an emotional component could be found in 37 out of 50 consecutive cases of asthma admitted to the Massachusetts General Hospital. The same finding was mentioned by Halliday[32] in a series of 30 patients. French and Alexander[33] have recently reported a study of 27 patients with bronchial asthma who were psychoanalyzed at the Chicago Institute of Psychoanalysis. Nineteen of these patients were under treatment for long periods, and the results have been reported in detail. The thesis advanced by this group of investigators is that asthmatic patients tend to respond to increased respiratory stimulation with asthmatic attacks. Hence, attacks follow situations or experiences that induce respiratory stimulation, such as intense emotion, muscular exertion and hurry. They also note the paradoxical observation that, in some cases, intense emotion has been known to bring about the cessation of an attack. As a tentative explanation of the paradox, French and Alexander suggest that the precipitating situations are those in which the patient "must suppress his emotion or in which he finds himself completely helpless to give adequate expression to it." They refer to the observation of other authors[31] that in cases in which the attack ceases on sudden emotion, adrenalin is mobilized in the blood stream; this mechanism apparently does not operate during the emotional conflict induced by the precipitating situation. From their analytic material, they find that the conflict situation relates to earlier situations that threaten to separate the patient from a female figure—a mother figure. The patient responds to this state of helplessness by an asthmatic attack, which according to these authors has the symbolic significance of a suppressed cry.

Deutsch[34] has postulated that the asthmatic patient undergoes a development characterized by an "affection" of the respiratory apparatus in early childhood associated with certain emotional factors at that time, emotional upsets in childhood, acting as conditioning factors, and the development of a marked dependence on a hated, domineering and aggressive mother.

Rogerson, Hardcastle and Duguid[35] report that practically all their asthmatic children were characterized by marked anxiety and lack of self-confidence. In the adult group, French and Alexander[33] found that their patients all suffered from a deep-seated insecurity and a more or less intense need for parental love and protection.

Atopic dermatitis. Atopic dermatitis is another chronic illness in which there are marked exacerbations and remissions. Most of the patients with this disturbance show sensitivity to specific allergens, and many have personal or familial histories of other allergic disturbances. Becker[36] has repeatedly pointed out that fatigue may play a major role in the etiology through its effect on the underlying "protoplasmic irritability," which, according to him, is constitutional. Stokes[37] has emphasized the relation between skin disturbances and psychosexual difficulties. Other workers have pointed out the significance of blushing,[38] exhibitionism[39] and the need for self-punishment.[40]

Greenhill and Finesinger[41] have found that situations dealing with work problems, family difficulties, psychosexual problems and changes in the

physical environment were associated with the exacerbation of symptoms. In this respect, the results confirm earlier studies of Becker and Obermayer.[23] These events were associated primarily with feelings of hostility, insecurity and depression. On the other hand, a smaller series of patients with lupus erythematosus discoides also showed a relation between situations and exacerbation of symptoms. This correlation was not nearly so striking as that in the atopic patients. The patients with atopic dermatitis had the characteristics of the compulsive-obsessive type, as well as difficulty in their relations with other people. There was a great incidence of feelings of hostility rarely shown in overt action. These patients were sensitive and tended to suppress feelings of anger. They entertained feelings of inadequacy, lacked self-confidence and were depressed and notably shy.

Other diseases. Certain studies have been concerned with urticaria,[42] angioneurotic edema,[43] hay fever[42] and the common cold.[44] Saul and Bernstein[42] believe that states of repressed, intense, frustrated longing are of primary importance complementing allergic factors. They also mention the interesting fact that urticaria appeared in 1 case when weeping was repressed and often terminated when the patient wept. Saul[42] has more recently confirmed the role of repressed longing in cases of hay fever and common cold.

Cardiovascular Diseases

Some of the earliest observations deal with the effects of situations and emotions on the cardiovascular system.[45] Acute cardiac and cerebral insults have been repeatedly described following emotional outbursts. In some cases, excitement and anger apparently bring about a rise in blood pressure, which causes breaks in peripheral vessels already weakened by an existing lesion. Likewise, acute transitory changes in blood pressure,[46] pulse rate[47] and cardiac output[48] are known to be associated with disturbing situations and with various emotions. Similar episodes are known to produce exacerbations in other illnesses, such as Raynaud's disease[49] and essential hypertension,[50] in which a vascular lesion already exists. Distinct personality trends have been described by Hamilton[51] in patients with elevated blood pressures.

The more detailed studies are concerned with essential hypertension. It has been suggested that essential hypertension is associated with unstable and tense personalities. The behavior of such persons is characterized by increased psychomotor activity.[52, 53] Alexander[54] and Saul[55] have studied several patients psychoanalytically in whom a diagnosis of essential hypertension was made. They state that the basic problems in these patients are concerned with attempts at handling their dependence. This dependence has its origin in an early relationship to a dominating parent, and leads to the formation of a pattern of general behavior to which the patient adheres thereafter. It is this submission to authority that the patient struggles against with rebellion and hostility. The conflict centers about the expression or repression of this hostility. During periods when either the dependence or the hostility could be gratified, the blood pressure was markedly lower. This formulation has been confirmed by Miller[56] in a study of psychotic patients with high blood pressure.

Endocrine Disturbances

Numerous studies in the literature deal with the relation between various endocrine disturbances and the psychoses.[57, 58] The effects of adrenalin on psychoneurotic patients, especially in anxiety states, has been investigated.[59] This whole field has been reactivated by the development of new and accurate methods of measuring estrogens, androgens, gonadotropin and pregnanediol, and by the more current study of vaginal smears. Correlations have been drawn between various phases of the menstrual cycle and instinctual drives, types of phantasies and dream productions.[60] The relation between androgens, estrogenic substances and the clinical picture is reported in studies on homosexuality[61, 62] and hermaphroditism.[63]

Of the various medical illnesses associated with endocrine disturbances, the most work has been done on hyperthyroidism (Graves's disease). As a result of studies in several large series of cases,[64, 65] it has been established that emotions associated with sudden fright or other psychic trauma frequently precede the onset of the illness. The appearance of exophthalmos and enlargement of the thyroid gland can appear within a few hours after the fright. Yet, according to Rahm,[66] these acute situations play a less important role in the precipitation of symptoms than do chronic worries or continuous anxiety. Little work has been done on the personality of patients with hyperthyroidism.[67]

Rheumatoid Arthritis

In rheumatoid arthritis, one is dealing with a disease of unknown etiology characterized by exacerbations and remissions. Although the factors playing a role in the onset of the disease and its exacerbations are unknown, some authors have suggested that emotional disturbances, anxiety and worry play a significant role.[68] Cobb, Bauer and Whiting[69] found that in a series of 50 patients with typical rheumatoid arthritis, a significant relation between disturbing situations and the arthritis occurred in 60 per cent. The situations

found alone or in combination included financial distress, family difficulties, the loss of a parent or spouse and unfaithfulness of a married partner. The effect involved was usually that of worry. Further studies on the personality of these patients are still in progress.

Epilepsy

Among a long list of the factors that play a role in producing convulsions, Cobb[70] has listed emotional shock as one that is effective in producing vasoconstriction. He mentions that fright, anger and other strong emotions may cause pallor of the face and changes in circulation elsewhere in the body. In a study on 36 patients, Fremont-Smith[71] found a direct relation between emotional tension and one or more of the major convulsions in two thirds of the cases. In several of the patients, all or nearly all the attacks had been immediately preceded by a strong emotion, usually that of fear, anger or frustration. Fremont-Smith was able to precipitate major or minor attacks in 8 of his patients by a discussion of the emotional difficulties. He concludes that, in many cases, the emotional tension acts as a precipitating factor for convulsive seizures, even though the patient may be unaware of this relation. Further studies on the unconscious mechanisms associated with fits have been reported by Kardiner.[72]

Miscellaneous Diseases

The above summary deals briefly with some of the more complete studies in psychosomatic medicine. The literature contains reports dealing with many other varied conditions, such as anorexia nervosa,[73] glaucoma,[74] sciatica,[75] diabetes,[76] heart disease[77] and even fractures.[76] The development of greater interest in these problems has brought with it an ever-increasing number of observations in medicine and its specialties.

Therapy

Therapy in psychosomatic medicine is similar to that used in the treatment of the psychoneuroses. The symptom can be considered a reaction of the patient to a stimulus, which may be simple or complex, and may be known or unknown to him. Psychiatric therapy attempts to modify the stimulus or the person reacting to the stimulus, or both. In many cases, modification or removal of the stimulus — that is, changing of the situation or removal of the patient from the situation — has been of therapeutic value. Other psychotherapeutic efforts have been directed toward changing the patient to enable him to withstand any situation without the need for pathologic reactions. Two methods are employed for this purpose. The first makes use of reassurance, suggestion, persuasion and even hypnosis, and as such is very closely bound up with the relation between the physician and the patient. The success or failure of this procedure goes hand in hand with the vicissitudes of the doctor-patient relation. The patient acquires no understanding of the factors involved, and his improvement remains associated with the magic power of the physician. The second means of change depends on the acquisition of insight and understanding on the part of the patient into the factors associated with the onset and exacerbation of the symptoms. This is accomplished by the use of either distributive analysis or psychoanalysis. In the former, the physician makes use of discussion that is based on the patient's modes of reaction and on his methods of handling difficult situations, especially those that seem to have a direct relation to the complaint. In psychoanalysis, emphasis is placed primarily on the uncovering and understanding of earlier modes of reaction, unknown to the patient. Therapeutic successes have been claimed by the proponents of all the therapeutic methods mentioned. As yet, no single approach has completely won the field. This fact alone suggests that considerably more effort must be expended in the future before a universally accepted therapy is developed.

Summary

Psychosomatic medicine deals with medical disturbances in which situational and emotional factors play a role in either the precipitation or the exacerbation of symptoms. The situations are, as a rule, associated with the unpleasant feelings of fear, anxiety, guilt, resentment, frustration and longing. These illnesses are found in persons who have conflicts in reference to the expression of hostility and anger; most of them do not have the frank symptoms of the psychoneuroses. Many studies indicate that these are people with obsessive tendencies who tend to ruminate over their difficulties and find it impossible to resolve them on account of indecisions. It may be that these tendencies present constant stimuli to the autonomic nervous system and eventually lead to chronic irreversible reactions in the end organs, resulting in a pathologic process. The fact remains that therapy has lagged far behind the understanding of these problems. Yet, at the present stage of information, the only practical approach in many illnesses appears to be that of psychiatric therapy. This is especially true in situations in which medical therapy as such has failed or is still lacking. The inadequacy of psychotherapy in many cases is a challenge toward improving

present methods or toward developing new methods. The value of psychotherapy, promising as it seems at present, can be established only through carefully controlled studies. This is the task of the future.

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THERAPEUTIC PROCEDURES IN PSYCHONEUROSIS*

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PROCEDURES in the treatment of psychoneurotic conditions have not reached the simple level of known indications and expected results that has been attained in chemotherapy. Knowledge in the treatment of disease usually takes great strides forward when the disease can be reproduced in laboratory animals. Pavlov[1] was able to reproduce in dogs psychologic conflicts that made them behave like persons suffering from neuroses. He demonstrated pathologic nervousness and sleepiness. Liddell et al.[2] have similarly produced enduring derangements of behavior in sheep by a combination of stimuli and have treated them successfully with bromide medication. Some of their sheep developed a cardiac disorder shown by a rapid and irregular pulse brought on by stimuli that had no effect on normal animals. The animals were "conditioned," that is, taught to make discriminations between stimuli. When this process of discrimination is refined, — when it is made difficult by delay or interruptions, — neurotic behavior develops.

Maier[3, 4] and Cook[5] have carried out similar work with rats, and at a recent meeting of the American Psychiatric Association, Massermann[6] presented evidence of neurotic behavior in cats that was produced by exposure to psychic trauma, which consisted in an annoying blast of air when, after having completed a task and opened a feedbox after a warning light had flashed, they were enjoying their reward and the satisfaction of their desire for food. He tried, and found successful, four different means of therapy: retraining by petting and reassurance, reinforcing and making inescapable the conflict situation, increasing the desire and strengthening the stimulus.

In human beings, the experimental production of neurosis and subsequent therapy have, for obvious reasons, not advanced so far, but laboratory research is stressed in clinics such as the Department of Psychiatry of the Massachusetts General Hospital.

A good many experiments were carried out years ago with hypnosis, by which it is possible to produce paralysis, anesthesia and changes in the skin capillaries and even minor changes in visceral functions (Charcot[7] and Bernheim[8]). In addition, there are observations about events and their effect on the incidence of neuroses. The number of neurotic conditions during World War I increased vastly, whereas the number of schizophrenias remained the same, and the observations that are already being collected about the present war again throw interesting light on the effect of certain types of experiences on subsequent behavior. Mira,[9] for example, mentioned first — and it was later restated by Miller,[10] Gillespie[11] and Ross[12] — that the neuroses that might be expected to develop under the intense experiences of total war do not appear if the person has no possibility of securing refuge in a safe area but must instead remain in the situation. Furthermore, it has been found that separation of children from their families is much more effective in producing psychoneurotic disturbances than the experience of actual bombing.

None of these observations have up to now been systematic enough to suggest reliable systems of therapeutic procedures, and different psychiatrists still vary in their indications and choices of method. The powerful influx of a great deal of psychologic theory, which came about through the psycho-

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analytic school and the psychobiologic school, has led to a whole new jargon that has served only to alienate the medical man from the whole work of psychiatric treatment. He has been content to develop his own trial-and-error procedures or to refer to a psychiatrist all the problems that made him feel uncomfortable, stopping his interest in the patient at that point. Psychotherapy was, however, first practiced by medical men, and one of the greatest contributors to the understanding of hysteria, Charcot,[7] made all his demonstrations in the medical clinic.

In this presentation, an attempt is made to present very simply the methods used in the Out Patient Department of the Massachusetts General Hospital, the indications under which they are applied, and the success obtained with them.

Diagnosis

Diagnosis necessarily precedes a decision regarding therapeutic approach. At present, the neuroses are classified as reactive depression, anxiety neurosis, hysteria, obsessive neurosis and hypochondriasis. It will be noted that neurasthenia is not mentioned; this condition, often labeled neurocirculatory asthenia, has in many cases been found to be either a mild depression or a mild anxiety state, or an infectious or hormonal disease. The other conditions may be briefly described as follows:

Reactive depression. The patient does not necessarily cry. The outstanding symptoms are slowness, inability to concentrate, hopelessness and, often, bewilderment. Medical disorders that the patient may have at this time — for example, asthma and gastrointestinal disturbances — may be aggravated. Some practice is necessary to recognize this condition because the patient often succeeds in his effort to hide his distress.

Anxiety neurosis. The picture is one of acute attacks with marked visceral disturbances (heart action, respiration and gastrointestinal function) and an intense subjective distress referred to as fear or nervousness. The free interval between attacks may be one of exhaustion.

Hysteria. This term is perhaps the most abused in the nomenclature of the neuroses, any dramatic behavior being described as hysterical. Among psychiatrists, it means rather a condition in which one finds paralysis, weakness, aphonia, vomiting and bladder disturbance without a discoverable lesion. It is usually accompanied by a striking absence of anxiety, even though the patient, on study, is found to live in a distressing situation. These pseudoneurologic symptoms characterize a large group of war neuroses, but under peacetime conditions they are seen chiefly in women.[13]

Obsessive neurosis. This is usually well understood: preoccupation with foolish thoughts or the necessity of carrying out absurd or childish actions disturbs the patient.

Hypochondriasis. An important distinction must made between anxiety neurosis, with evidence of genuine disturbance in the circulation and the visceral organs, and hypochondriasis, in which the patient complains of peculiar sensations in his body, such as changes in the shape and size of his head, and points them out to the physician as suggestive evidence of serious illness.

Treatment

After the condition with which one is dealing has been ascertained, the next step is to choose a suitable therapeutic procedure. The methods may be divided as follows: suggestion, especially hypnosis; reassurance; exploratory procedures in which one attempts to ascertain the distress under which the patient is expected to be laboring and tries to solve this problem with him; medicinal treatment; and, finally, guidance and care by social-service assistants. The exploratory procedures form by far the largest number. Because of the difficulties and skills involved in this method, it must often be delegated to a trained psychiatrist, who is familiar with the modes in which a person interacts to his environment, especially to other persons; yet it is essential for the general physician to know and use this procedure.

If a disorder is regarded as psychogenic it is considered to be due to conflicting stimuli arousing overwhelming emotions that the patient cannot handle with his own resources. The patient's symptoms, which to him represent disease, must be translated into a new context in which they will be recognized by both patient and psychiatrist as part of a disturbed emotional response to a difficult situation. Only if one succeeds in doing so, may the patient be successfully reassured about his illness, even though his difficulty may not be solved and even though he may feel upset. (Ross has given practical suggestions concerning how to do this successfully.[12]) Furthermore, only after the patient has found a solution of his predicament may he hope that his symptoms of anxiety and depression will disappear.

The successful completion of an exploratory procedure involves the discovery of a patient's predicament and a demonstration of its tangible solution. At first glance, this may appear a hopeless task. There is the necessity of winning over the patient for the psychiatric procedure and, after doing so, of making it possible for him to have free expression. Many failures occur at this point. Experience has shown that a number

of simple rules applying to the first interview may make all the difference between success and failure. The first of these is that the patient must believe that he is guaranteed reasonable privacy; this does not involve the privacy of a confessional. The patient is usually willing to waive this right if he knows how far his problems will be discussed and if he is assured of the bona fide interest of other listeners. Secondly, the patient must be assured that the physician has no moral bias and is willing to consider with him accounts even of events about which he feels very guilty or has broken taboos. Furthermore, the patient must be assured that the physician will not take advantage of him — that is, overrun him by authoritative advice when he would like to have an opportunity to make up his own mind. And, finally, the patient must have an opportunity to lead the way in the interview. This has led to a discarding of the ordinary systematic questioning in favor of a method by which material is collected in a somewhat erratic manner, following the lead of the patient and filling in the gaps as need be. Deutsch[14] has described this procedure in great detail.

If these rules are observed and if one avoids compromising statements, not only may one succeed in obtaining the significant story of the patient's difficulty but also the solution may present itself to the patient without advice from the physician. In the presence of a trusted expert, the patient is likely to penetrate farther in his search for a solution, having stopped short at painful thoughts in his previous unaided ruminations.

It has been found desirable to separate this first step of the treatment into two phases: a brief preliminary interview, to get acquainted and to learn the essential complaint; and a second interview in which the patient is dealing with a known person with whom he may be confidential.

A frequent, false impression is that patients who have a large number of complaints and tell a great deal about their difficulties are the ones who benefit most. Much of the material may be quite insignificant. To understand which material is of consequence and which is not, some experience is needed in watching the patient's emotional response during the discussion, his hesitations and his labored efforts at communication. Apparently, only experiences that are described with some recurrence of emotion can be utilized for therapy. Of all the innumerable circumstances, it can be said that little turns out to have therapeutic moment except a situation that has aroused an overwhelming reaction of one of five major patterns of emotional response: grief in response to loss; anxiety in response to threat or temptation; rage in response to provocation; and the two appetites, those of hunger for food and the need for sexual expression. The situation that aroused the emotion may be obvious or may become manifest only after considerable search. A person with hysteria of long duration may describe his life as free of stress and strain, and a person with an obvious anxiety neurosis may at first be completely unaware of any situation that should have aroused his rage or fear; yet it is always there, and if, after prolonged search, nothing along this line can be found, one is tempted to revoke the diagnosis and to consider seriously the presence of a structural or chemical disorder such as hyperthyroidism or a deficiency state.

The situation that arouses the abnormal response when once found may be strikingly simple and offer itself for easy remedy, as in the following case.

CASE 1. A 38-year-old fireman was referred 1½ years after he had fallen from a ladder and sustained minor hand injuries and a fracture of the right arm. Although the bone lesions had healed without defect, he was still complaining of pain in his arm and, in addition, had received compensation for nervous shock, symptoms of anxiety having developed about 4 weeks after the accident.

Exploration showed that this man had never had any serious illness, that he had in no way shown signs of "neurotic make-up," and he resented being questioned by a psychiatrist. It was discovered, however, that after the accident his superintendent had made arrangements to have him put on light duty and had given him a job as a telephone operator. Being accustomed to vigorous activity and to "showing off," he felt stifled. He then started to tell stories of former exploits and had to be repeatedly reprimanded by his superior. Being stalled from his usual activities, the patient became unduly irritated and had to refrain a good many times from outbursts of violence against the man who was guaranteeing him his compensation. Finally, the superintendent enclosed the telephone in a glass box, and thus effectively prevented him from any further verbal activity with his friends. It was then that the severe symptoms of anxiety developed.

With a knowledge of this state of affairs, it was obvious that the well-meaning rest cure had turned out to be the pathogenic agent and that winning the patient to attempts at renewed vigorous activity would be very likely to restore his equilibrium. He was advised to change his job and to apply for a position as probation officer, which he did successfully. At a subsequent visit 3 years later, he reported that he had been symptom free and that he had gladly given up his compensation for his new chance for enjoyable work.

Sudden, severe grief and sudden fright during accidents, as well as sudden prevention from the execution of an act of rage or an attempt to satisfy one's sexual urge, may be followed directly by a psychoneurosis. One is likelier to find, however, that a series of minor disturbances, to which the patient has not responded, may finally accumulate to such a degree that only a very violent or intense emotional reaction can offer adequate discharge.

CASE 2. A 27-year-old cranberry picker was referred 2½ years after sustaining a Pott's fracture of the right forearm while cranking a tractor. He complained of cramplike contractions of the muscles of the forearm, which led to a forced closure of his hand into a fist. Although his original fracture had healed, "nervous symptoms" had developed shortly after his return to work, and he considered himself permanently disabled by this disorder.

Exploration showed that the cramp of the hand occurred only when the assistant superintendent was walking by, that the same assistant superintendent had ordered the patient, after hours, to crank the car, an act that had produced the fracture, and that this man had provoked him on innumerable occasions to violence. The patient had been unable to give in to these because he was on court parole for former brawls at the village tavern and had recently married a "reformer" wife, who daily reminded him of his duty to keep his job for the sake of their child. He found to his own surprise that the cramp of his hand was really a fist about to be launched against the hated assistant superintendent.

The symptom disappeared only after the company had given him a "token" advancement, which somewhat improved his status in relation to the assistant superintendent.

Some such change in environment is often necessary to permit the patient to adjust himself without his symptoms. Even if the patient is willing to adjust himself to the situation again, a face-saving device of some sort is necessary. Frequently, teamwork with a psychiatric social worker is indispensable to bring about this change, which may be small indeed but which must exactly fit the patient's needs.

In the course of the exploration, it may become obvious that the patient habitually gets into situations that are very difficult for him to meet because of poor training or inadequate personality. If this is so, the simple exploration will not be satisfactory, and a more prolonged and effective method of altering the personality will be necessary. Patients with this type of condition must often be referred for psychoanalytic treatment. In severe conditions, such as hypochondriasis, it may be necessary to regard the patient as an object for care and guidance who may have to be looked after in a carefully planned family setting.

Fortunately, a large number of patients do not show any serious personality defect, but have developed their psychoneurotic inadequacy under the impact of a very difficult situation. If the situation is severe enough, the condition presented may constitute a psychiatric emergency, and special measures are indicated.

Under peacetime conditions, such measures are called for in the severe reactive depressions and the markedly incapacitating hysterical reactions with such symptoms as aphonia, paralyses and amnesia. In wartime, these reactions occur in persons who witness violence and destruction and who should, with the greatest expediency, be restored to their normal level of efficiency. For this purpose, a number of procedures have been developed, among which hypnosis finds its proper place. Hysterical monoplegias respond very well, as do states of anxiety after a severe traumatic experience. Hypnosis may be helped by the administration of sedatives, such as Pentobarbital and Sodium Amytal. Curiously enough, there is one other way of restoring such patients to proper functioning; by provoking in them an emotional reaction of the same degree as the previous traumatic reaction. This principle used to be applied by means of electric shocks, faradic current being employed, or by bringing the patient into frightening surroundings. These procedures have largely been abandoned. However, it may be advisable to use a chemical agent to produce a storm in the autonomic system.[15] Thus, one may, to good advantage, give intramuscular injections of 20 to 25 mg. of Mecholyl,[16] followed by appropriate commands: for example, to make renewed efforts at using a paralyzed extremity and — even more important — to cease interfering, by undue contraction, with its proper functioning.

It is sometimes possible to use the emergency procedures as an opportunity for reliving the disturbing situations and for verbally expressing the emotional reaction connected with them. In this form, the so-called "cathartic method" initiated by Freud and Breuer has survived.

In most emergency procedures, however, one cannot get acquainted with the predicament. One pushes the patient back into a situation that once, at least, was intolerable for him. In war, this is inevitable; in peace, often enough, the situation has changed during the patient's hospital stay so that it has become more bearable.

However, in patients who are especially vulnerable,— that is, those who are especially easily aroused to overwhelming emotions,— one may have to use a procedure which confronts the person with the need for discussing repeatedly a disturbing situation that he has to meet. Freud discovered that recalling a painful experience is likely to bring with it a return of the emotion linked to this experience. This return is used in a skillful manner in psychoanalysis to "desensitize" the patient and to steel him to cope with the ordinary occurrences that he will have to meet. Since some persons, owing to fear that they may have to meet difficult situations, have remained at an infantile level of emotional development and have missed a great many opportunities to strengthen and test their ability to withstand temptation and certain conflicts, psychotherapeutic procedures may well attain an educational value.

Numerous explorations have shown that a patient exposed to severe grief may temporarily be able to block his reaction in some manner. This reaction, however, may occur years later at the occasion of suffering a relatively innocuous loss. In other conditions, the emotional response may be delayed. It may also be distorted, and thus in grief a person who tries to extricate himself from his bondage to a deceased person may temporarily withdraw all his interest and may experience the world as unreal until his mourning is over.[17] Since grief reactions, whether displaced or not, are usually self-limited, the task of the psychiatrist is often restricted to relieving the tension by mild sedation with Sodium Amytal or by stimulation with amphetamine (Benzedrine) sulfate.[18] It may be pointed out that exploration can be performed only if the patient is not too much disturbed and if he is not too disinterested, and medical agents may be employed to maintain the most suitable level of emotional tension; thus, it is futile to discuss with a severely depressed patient the reason for his mourning.

One of the most striking depressive reactions, with agitation, insomnia, restlessness and hopelessness, is often found after surgery, particularly after pelvic operations in women, after tooth extractions and after eye operations.[19] This reaction is not likely to occur before a free interval of four weeks, and may then go on for years, the patient being entirely unaware of the situation that has aroused the overwhelming emotion. Exploratory therapy tracing back the emotional response has led to the discovery that the rage response is the outstanding reaction. If the patient is helped to handle his unwarranted rage, readjustment occurs with surprising ease. A number of middle-aged women who were considered to suffer from melancholia have responded to this form of psychotherapy with enduring success after four or five interviews.

Results

This review of methods may be augmented by a report about follow-up observations. Such observations are admittedly difficult because they depend on the goal that one has placed before oneself. Also, the reports of the patients and their families are often unreliable. One may, however, obtain a rough estimate if one agrees that treatment should be regarded as successful with patients who feel satisfied, are able to work and who are not handicapped in their social and sexual adjustment.[20] If they still have their symptoms but do not let them interfere with their work, they should be considered improved only. Everything else, for the purposes under discussion, has been considered failure.

Of 200 patients who were seen between October 1, 1937, and October 1, 1939, in the Psychiatric Out Patient Clinic of the Massachusetts General Hospital, and who were seen again a year after discharge, 162 were satisfied, and 38 considered the treatment a failure. These good results may partly be due to the fact that we selected patients who, experience had shown, would respond to treatment. In the progress of our work, we began to realize that the anxiety states, the reactive depressions and hysteria were suitable for the type of therapy available in our clinic.

The treatment of hypochondriasis proved unsuccessful in almost every case; obsessive neuroses improved only temporarily.

The patients with anxiety neuroses turned out much better. The explorative technic was used on all of them; some lost their symptoms after only one interview, and others, especially those who had phobias, had to have more than fifteen interviews. Several anxiety neuroses were temporarily relieved by amphetamine; some of them responded with a paradox reaction, becoming much worse.

The care of patients with depression was very successful, but it is suspected that some of the anxiety neuroses that had a depressive coloring improved not so much because of our efforts as because of the self-limiting character of a depressive reaction.

The patients with hysteria showed a mixed picture. Severe hysteria, with a history of long-standing infantilism, and typical hysterical personality, does not respond well to general hospital psychotherapy. This seems to be the domain of the prolonged treatment and psychoanalysis, which may succeed with some patients when other methods fail, but even this procedure does not always guarantee success. Patients with hysteria who have undergone a large number of operations are also difficult; we have failed in almost every one of them. On the other hand, patients with limited hysterical symptoms, such as monoplegias, may lose their symptoms after one or two interviews or in response to one of the more forceful procedures, such as hypnosis or the use of Mecholyl.

If our findings are compared with those in other reports, it is noted that the recovery rate with systematic treatment varies but little from clinic to clinic, and that the percentages of recovery or marked improvement are reported as 70, 82 and 87.[21] This looks very encouraging, but one must take into account the natural recovery rate of the psychoneuroses. Landis[22] has collected statistical data from numerous hospital sources and has stated that 62 psychoneurotic patients out of every 100 are discharged from state hospitals within a

year. This, of course, does not mean that they are recovered or symptom free but rather that they have been able to be returned home. Controlled series of an adequate sort giving a natural history of the neuroses are not available as yet.

* * *

It is possible to learn psychotherapy. Physicians in training witness interviews for about a month and then do explorative work themselves with patients, discussing each interview with an older man. From this experience, they become acquainted with the pitfalls of the methods and avoid the two most serious dangers of psychotherapy: getting involved in the patient's emotional reaction to the therapist and driving the patient into "acting out," in his social life, primitive reactions that may have been discussed in the interview. In consequence of these reactions, a poor psychiatrist may be as dangerous for a patient's social life as a poor surgeon for his physical life. A young physician who is not at all suited for psychotherapy very soon becomes bored with it. A certain amount of ability to listen and a capacity to let the other fellow have his say are prerequisites for this work.

In our clinic, in addition to young psychiatrists in apprenticeship, we also train a number of physicians whose primary interest is in medicine rather than in psychiatry but who want to be able to use psychotherapeutic methods intelligently in general practice and to learn to recognize cases that should be referred to a specialist for more intensive treatment.

At present, the war situation and the intensified requirements of industry, in which every loss of efficiency due to neurosis counts double, require more than ever the psychotherapeutic efforts of the general practitioner. One of the most challenging problems is presented by the 8 to 11 out of every 100 selectees who are now being rejected because of psychiatric difficulties, for whom methods of rehabilitation are being sought.

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CLINICAL FEATURES OF PANCREATIC LITHIASIS*

Report of Two Cases

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THE formation of stones in the pancreas has been recognized since 1667. The presence of stones in the pancreas of a patient with diabetes was first reported in 1788,[1] when a direct relation between pancreatic stones and diabetes mellitus was suggested. Further interest in this relation was aroused in 1901, when Opie[2] stated that stones may lead to atrophy of the pancreatic parenchyma, although the islet cells are not affected. In 1920, Barron[3] pointed out that atrophy of the pancreas, resulting from long-continued obstruction of the ducts by stones, is not associated with diabetes mellitus provided that the islands of Langerhans remain intact. This observation served as the stimulus for the work that resulted in the discovery of insulin.[1]

Despite the long history of the subject and its potential importance, it has generally been believed that pancreatic lithiasis is relatively rare. That this is not entirely true is shown by a few recent reports. In 1936, Mayo[4] found 25 cases listed in the records of the Mayo Clinic, and in the next four years, Snell and Comfort,[5] conducting a systematic search, discovered 18 additional cases. Opie,[6] in 1500 necropsies, observed only 2 cases of pancreatic stones, and Dillon[7] found only 2 among 2800 autopsy records. Lüdin,[8] on the other hand, by very careful examination of each pancreas, noted 28 cases in a series of 542 autopsies. Warren[9] reported a frequency of 3 cases in an autopsied series of 300 patients with diabetes. Smith and Bonis[10] found, in the course of five months, 3 cases in a series of 240 roentgenologic examinations that included the pancreatic area. Finally, Rockwern and Snively[1] saw 2 cases within a month at the Cincinnati General Hospital, although only 3 had occurred among 7402 post-mortem examinations at that hospital in the preceding twelve years.

More and more cases are being diagnosed during life as the value of taking a flat film of the abdomen in patients with abdominal pain gains wider appreciation. It has been pointed out, however, that a barium meal can easily obscure the presence of pancreatic stones.[1] At the Boston City Hospital, the diagnosis was made in 3 cases from 1934 to 1941 — at operation in 2 and at autopsy in 1. During 1941, 3 cases of pancreatic stones were recognized among 700 autopsies. Two additional cases were observed while on the wards of this hospital at the same time. The diagnosis in one rested on the roentgenogram; in the other, the roentgenographic findings were confirmed by palpation of the pancreas at laparotomy. Because we were able to study the pancreatic ferments of these patients before and after stimulation with Mecholyl (acetyl-beta-methylcholine chloride) and because few cases have been studied with the aid of such pancreatic stimulants as secretin and Mecholyl, we believe that our data warrant reporting.

To obtain the duodenal juice uncontaminated by gastric juice, the method described by Agren and Lagerlöf[11] was used, care being taken to place the tube under direct fluoroscopic control. Mecholyl was used to stimulate the external pancreatic secretion according to the method of Comfort and Osterberg.[12, 13] Amylase activity was determined by the method of Agren and Lagerlöf,[11] and lipase activity by that of Crandall and Cherry.[14]

CASE REPORTS

CASE 1. Mrs. J. B., a 35-year-old woman, was admitted to the hospital in July, 1941, complaining of pains in the legs, with weakness and inability to walk, of 2 months' duration. For 3 months, she had experienced anorexia, nausea and vomiting, especially in the morning, associated with more or less constant, but not usually severe, pain in the midepigastrium and left upper quadrant of the abdomen.

The patient had been admitted to this hospital in 1937, complaining of pains and weakness in the legs for a month and of midabdominal pain and vomiting for 6 days. Physical examination at that time revealed emaciation, scaling skin over the forearms, a beefy red tongue, an enlarged, firm, nontender liver, bilateral foot drop, absent tendon reflexes, loss of position and vibration sense, and tenderness of the calves. On a high intake of vitamins, carbohydrate and protein, the patient gradually improved over a period of 15 weeks. The discharge diagnoses were as follows: chronic alcoholism; alcoholic gastritis; dietary and vitamin B complex deficiency, with emaciation; polyneuritis; stomatitis; fatty infiltration of the liver; and chronic pyelonephritis.

Physical examination at the second admission showed marked emaciation, a strong odor of alcohol, tremors of the hands, roughening and scaling of the skin, particularly over the dorsum of the hands and over the elbows, and multiple ecchymoses over the extremities. The tongue was smooth and red. The liver edge was firm, smooth and sharp, and was palpable 3 cm. below the costal margin. The abdomen was soft and extremely tender in the left

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upper quadrant. The feet were plantar-flexed and could not be voluntarily dorsiflexed. All tendon reflexes were absent. The calf muscles were tender to pressure. The blood pressure was 120/80.

The blood Hinton reaction was negative. The red-cell count was 2,700,000 with a hemoglobin of 9.8 gm., and the white-cell count was 9600 with a normal differential. The urine showed a specific gravity of 1.020, no albumin, sugar, acetone or casts, and 10 white blood cells per high-power field in the centrifuged sediment. The nonprotein nitrogen of the blood was 27 mg. per 100 cc. The serum protein was 5.2 gm. per 100 cc. The icteric index was 15. Urobilinogen was present in the urine in dilutions ranging from 1:20 to 1:40. The bromsulfalein excretion test of liver function showed 100 per cent retention at 5 minutes and 50 per cent retention at 15 minutes.

Because the patient developed an acute exacerbation of her chronic pyelonephritis during the 2nd week, a flat film of the abdomen was taken. No renal calculus was noted, but irregular areas of calcification were revealed that extended across the upper abdomen, both to the right and to the left of the midline, at the level of the first and second lumbar vertebras. These areas followed the general outline of the head and body of the pancreas (Fig. 1),

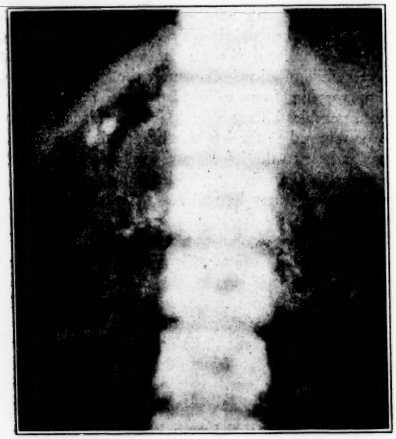

FIGURE 1. *Case 1.*

This flat film of the upper abdomen shows many fine calculi in the tail, body and head of the pancreas.

and were later shown by gastrointestinal roentgenograms and by fluoroscopy during duodenal intubation to lie enclosed within the curve of the duodenum.

Determinations of the pancreatic enzymes, amylase and lipase, were carried out on two occasions, 19 days apart, by the methods noted above. The results are listed in Table 1. The serum lipase activity was 1.18 expressed in cubic centimeters of 0.05N sodium hydroxide (average activity ranges between 0.2 and 1.5 cc.). There was no diarrhea, and examination of the stools stained with sudan III showed no increase in fat content. Glucose tolerance was determined with 100 gm. of glucose by mouth; the values, expressed in milligrams of glucose per 100 cc. of blood, were: fasting, 83, 1 hour, 265, 2 hours, 274, and 3 hours, 263.

On a regimen consisting of a high-carbohydrate, high-protein and low-fat diet, supplemented by brewers' yeast, thiamine hydrochloride, niacin (nicotinic acid), Vegex

TABLE 1. *Results of Continuous Drainage of Fasting Duodenal Juice for One Hour before and One Hour after Mecholyl.*

DATA	VOLUME *cc.*	AMYLASE *gm. of maltose*	LIPASE *cc. of 0.05 N NaOH*
Normal values			
Before Mecholyl	10–120	6–250	70–10,000
After Mecholyl	10–180	30–500	2000–18,000
Case 1			
Before Mecholyl	31–54	3.6–18.8	490–1310
After Mecholyl	55–73	9.5–40.2	1790–2490
Case 2			
Before Mecholyl	78–80	2.2–27.5	960–1770
After Mecholyl	70–120	8.3–39.8	1360–2520

and ferrous sulfate orally, in addition to 5 cc. of crude liver extract intramuscularly twice weekly, the patient slowly improved over a period of 2 months. The liver receded to the costal margin, although she did not receive lipocaic. The bromsulfalein test eventually showed 80 per cent retention of the dye at 5 minutes and 30 per cent at 15 minutes. A biopsy of the liver, obtained at this time with the peritoneoscope, revealed only minimal traces of fat in the parenchymal cells with minimal increase in fibrous tissue. The red-cell count rose to 4,400,000 at the time of discharge.

CASE 2. Mrs. G. K., a 57-year-old woman, was admitted to the Third Surgical Service (Boston University) of the hospital in September, 1941, because of three attacks of severe, colicky, right-upper-quadrant abdominal pain, with associated vomiting during the preceding 4 years. Between attacks, she had suffered from abdominal bloating and gaseous eructations after meals, particularly after spicy or fatty foods, and occasional mild diarrhea. During the year before admission, she had noted polyuria, polydipsia and a weight loss of 35 pounds. Because glycosuria and hypertension, as well as pancreatic lithiasis by roentgenogram, were discovered, the patient was transferred to the Fifth Medical Service for further study prior to operation.

Physical examination showed her to be obese and not acutely ill. The retinal arteries were narrow and tortuous, and the radial arteries were thickened. The heart was not remarkable. The blood pressure was 210/96. There was slight tenderness, but no spasm, in the right upper quadrant of the abdomen. The liver was not palpable.

The blood Hinton reaction was negative. The red-cell count was 4,500,000 with a hemoglobin of 12.2 gm. (Sahli), and the white-cell count was 7000 with a normal differential. The urine showed a specific gravity of 1.035, no albumin, acetone or bile, an orange reduction with Benedict's solution, and 1 hyaline cast and 2 white blood cells per high-power field in the centrifuged sediment. The nonprotein nitrogen of the blood was 30 mg. per 100 cc., and the fasting blood sugar 143 mg. The icteric index was 5. Urobilinogen was present in the urine in a dilution of 1:16. The bromsulfalein excretion test showed 45 per cent retention at 5 minutes and 5 per cent retention at 15 minutes.

A Graham test showed poor filling of the gall bladder with dye and failure to empty after a fatty meal. A flat

roentgenogram of the abdomen revealed several areas of calcification in the region of the head of the pancreas (Fig. 2).

Two determinations of pancreatic enzymes were performed 13 days apart. The results are recorded in Table 1. Stools stained with sudan III showed no excess of fat.

FIGURE 2. *Case 2.*
This lateral film of the upper abdomen shows two large calculi in the head of the pancreas.

While under observation, the patient had a severe attack of right-upper-quadrant colic, accompanied by fever and leukocytosis. The serum lipase during the attack was not elevated (0.73 cc. 0.05N sodium hydroxide).

After completion of studies and control of the diabetes by diet and 25 units of protamine zinc insulin daily, the patient was returned to the Third Surgical Service. Operation disclosed a large stone in the gall bladder, with a small stone and some gravel in the common bile duct. The liver appeared normal, and no biopsy was taken. The pancreas was not visualized. By palpation, however, it was considered to be atrophic, and several stones were easily palpable. No attempt was made to remove them.

DISCUSSION

The origin of pancreatic stones is not entirely clear. Because they consist of calcium carbonate and tribasic calcium phosphate, which are not present in normal pancreatic juice,[3] and because bacteria have been found in them,[15] it is generally assumed that infection of the pancreas causes an alteration in the juice, leading to the deposition of calcium salts.[5, 15, 16] In addition, stasis of the secretions in the ducts appears to be necessary, as Lazarus[17] found that stones could be produced in the pancreas of dogs only by a combination of stasis and infection. From this evidence, it has been inferred that pancreatitis and, possibly, cholecystitis and cholelithiasis are the major predisposing causes of the disease. However, few cases have a history of previous attacks of pancreatitis. There was no conclusive evidence that either of the patients in the cases presented above had ever suffered from acute pancreatitis, although the mid-abdominal pain and vomiting noted in Case 1 at the first admission could have had such a basis.

Many patients, however, show a coexisting cholelithiasis, although Snell and Comfort[5] found only 3 in their series of 18 cases. One of our patients (Case 2) had associated cholecystitis and cholelithiasis; the other had no definite symptoms of gall-bladder disease and showed no cholesterol or calcium bilirubinate crystals in the "B" bile obtained by duodenal drainage. Although evidence of cholelithiasis or pancreatitis cannot be ascertained clinically in many cases, at post-mortem examination the pancreas is frequently the seat of an inflammatory process that may be evidenced only by fibrosis and cystic changes at the time of examination.

The clinical diagnosis, although difficult, is probably often missed because it is not thought of. Upper abdominal pain is usually the leading symptom, varying from mild distress to severe colic that resembles biliary colic. However, it is likelier to be referred to the left side of the abdomen and may radiate to the left side of the back, to the left costovertebral angle or to the left shoulder.[5] Nausea and vomiting may be severe. Attacks seem to be induced by fatty foods, but are more frequently precipitated by alcoholic excesses than attacks of gallstone colic.[15] *Fatty diarrhea* is perhaps the most characteristic sign of the disease, but it has been noted in no more than half the reported cases and may be intermittent, occurring only after an episode of colic.[5] Enlargement of the liver may be another late sign of pancreatic damage. The work of Dragstedt et al.[18] suggests that this results from fatty changes in the liver consequent to deficient production of lipocaic by the pancreas. Diabetes mellitus, actual or latent, accompanied by abdominal pain of obscure origin, should immediately point to the possible existence of this disease. Finally, icterus occasionally occurs in pancreatic lithiasis. If this syndrome is kept in mind, and a flat film of the abdomen is obtained in suspected cases, the diagnosis should be made with greater frequency.

The chief difficulty in the clinical diagnosis of pancreatic stones lies in the frequent absence of unmistakable signs of pancreatic insufficiency. Coffey, Mann and Bollman[19] have shown experimentally with dogs that gross alterations of digestion, as manifested by steatorrhea and creatorrhea, occur only in the complete absence of the external pan-

creatic secretion from the intestine. Even small amounts of pancreatic tissue sufficed to maintain complete digestion in their animals. To facilitate the diagnosis of relative pancreatic insufficiency, when steatorrhea is absent, Agren and Lagerlöf[11] using secretin, and Comfort and Osterberg,[12, 13] using secretin and Mecholyl as pancreatic stimulants, describe methods for obtaining the external pancreatic secretion uncontaminated by gastric juice. The procedures give a roughly quantitative estimate of pancreatic output.

We used Mecholyl in studying the pancreatic-enzyme production of our patients. Each patient was examined on two separate occasions, since we have found that one test may give misleading low results that cannot be duplicated later. Table 1 shows that the amylase and lipase contents of the duodenal juices of both patients were in the low normal range. In each case, there was a significant increase in enzyme content after stimulation with Mecholyl, the only exception being the first lipase determination in Case 2. The results of these tests indicate that some pancreatic damage was present, yet not enough to lead to gross steatorrhea. The conclusion appears legitimate that the damage was directly connected with the calculi present, which caused obstruction of the ducts, with resulting atrophy of the acinar tissue. Lagerlöf,[20] Snell and Comfort,[5] Smith and Bonis[10] and Rockwern and Snively[1] found normal or low amounts of enzymes in their patients with pancreatic lithiasis.

Reference has already been made to the frequent finding of diabetes mellitus in association with pancreatic stones. Since the incidence of diabetes is greater in cases of longer standing, the implication is that it results from progressive destruction of the islands of Langerhans. However, it is remarkable that there may be no correlation between the degree of pancreatic damage and the severity of the diabetes. In fact, patients who appear to have extensive pancreatic destruction over a long period may show no sign of diabetes. Opie[2] commented on the case of a ninety-year-old man who had been in good health all his life despite the presence of steatorrhea for twenty years prior to his death; the patient had no symptoms or signs of diabetes, yet, at autopsy, the duct of Wirsung was completely blocked by a calculus, and the pancreas was almost wholly replaced by fat. Another man, who was 72 years old, had had fatty diarrhea for two years, but never had had glycosuria; the pancreas was entirely replaced by fat, with a large stone in the duct and smaller ones scattered throughout the gland. In a third case of pancreatic lithiasis, seen on the Third Medical Service of the Boston City Hospital before the cases presented above, the patient was a known diabetic who had been controlled for a year by 15 units of protamine zinc insulin. He gradually failed, complaining of mid-abdominal pain radiating into his left upper quadrant and back. The diabetes, during his final sojourn in the hospital, became less severe and was eventually controlled by 5 units of protamine zinc insulin daily. At autopsy, however, the pancreatic parenchyma was found to be about 95 per cent destroyed, being replaced by chronic inflammatory tissue and cystic, dilated ducts containing many irregular, rough stones.

So far as the enlarged liver that may be a late accompaniment of pancreatic lithiasis is concerned, we wish to point out that the patient in Case 1 showed a definitely enlarged liver, with decreased function of the bromsulfalein test. She was treated with a low-fat, high-carbohydrate, high-protein diet and a high-vitamin intake, rather than with lipocaic. Response to this regimen was quite satisfactory. The liver gradually receded to normal size, and a post-treatment biopsy showed only minimal amounts of fat and fibrosis. We concluded that the hepatic enlargement in this case was not due to lipocaic deficiency.

Although no attempt was made to remove the stones in either of our patients, surgery has frequently been employed successfully both to rid the patient of symptoms and to halt further destruction of the pancreas. Of 65 cases collected from the literature, 58 were treated surgically.[15] Schmieden and Sebening[21] call attention to 11 patients who were completely cured by removal of the stones. At the Mayo Clinic, when the diagnosis had been made sufficiently early, successful operations were performed.[5] The danger of postoperative pancreatic fistulas has been largely overcome by improved surgical technic, and reactivation of the pancreatitis or peritonitis appears to be rare.

In the symptomatic treatment of the disease, the use of dried pancreatic juice to correct the symptoms of pancreatic insufficiency has been of value.[5] Although the fatty liver in Case 1 did not require lipocaic, Snell and Comfort[5] found that it had a specific effect in at least 1 of their cases. The colic is usually treated with morphine, but ephedrine is worthy of a trial, since it diminishes pancreatic secretion. The primary treatment of this disease, however, is surgical.

Summary

Recent reports agree that pancreatic lithiasis is not excessively rare. The clinical diagnosis is becoming more frequent as roentgenograms of the abdomen are more widely obtained in cases of obscure abdominal pain.

Two cases are reported in which the diagnosis was made during life by roentgenography and confirmed in 1 case at operation. The degree of pancreatic insufficiency was determined by examination of the enzyme activity of the duodenal contents after stimulation with Mecholyl. Lipase and amylase activity fell in the low normal range. Steatorrhea was not present. One patient had cholelithiasis and frank diabetes mellitus. The other had a decreased glucose tolerance and an enlarged liver that showed improvement without the use of lipocaic.

The essential features of pancreatic lithiasis are discussed.

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MEDICAL PROGRESS

DISEASES OF THE THYROID GLAND

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SINCE my first report on this subject of three years ago,[1] a large amount of investigative work, both experimental and clinical, has been reported and must needs be digested. The large volume of such work is in part owing to the fact that many new approaches to the study of thyroid physiology, both normal and morbid, have recently become available.

For many years, one looked upon basal metabolic rate as the sole yardstick for measuring thyroid function. Then the determination of blood iodine levels made its appearance on the scene, and now such procedures as the measurement of thyrotropic hormone output in the urine, the collection of radioactive iodine by the thyroid, the effect of patients' serum upon the metabolism of test tissues, thyroid or other, the behavior of patients' thyroid when explanted in tissue culture and many other methods are available to him who would solve a hormonic riddle.

A report on progress in diseases of the thyroid gland in this year 1942 may properly take its departure from the thyrotropic hormone of the anterior pituitary, or as it is convenient to call it, TSH (thyroid stimulating hormone), because this hormone still is a center of interest, and the discovery of how it acts on the thyroid cells may elucidate some of the morbid hormonic patterns encountered in thyroid diseases.

To the reader interested in being brought up to date on the now vast literature on TSH, the article of the Australian, Lambie,[2] can be most heartily recommended. Lambie reviews the literature, giving a bibliography of three hundred and nine titles, and also reports observations of his own and discusses the relation of the hormone in question to clinical syndromes. He draws the broad general conclusion that the ultimate stimulus to the thyroid is chemical, not nervous, but this does not mean that nervous influences may not impinge on the thyroid, nerve-borne from hypothalamus to pituitary, humorally from pituitary to thyroid. With this concept, I find myself in substantial agreement. It provides an explanation

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for the paradox that whereas disturbed thyroid function may follow psychic trauma, experimental evidence is against any direct secretory innervation of the thyroid gland (Uotila[3]).

That a hormonic balance exists between pituitary and thyroid was indicated in my previous review. Salter[4] has given this the appropriate name of "pituitary-thyroid axis," a beneficent axis in health, but sometimes leading to mischief in disease, like a certain other axis, which need not be mentioned. The evidence that the pituitary through its TSH drives the thyroid cells to increased activity is so abundantly proven as to need no further discussion, and DeRobertis[5] has shown that changes in thyroid histology begin as early as fifteen minutes after the injection of TSH.

The evidence that the thyroid hormone inhibits the pituitary with respect to TSH secretion is also increasing (Reforzo Membrives,[6-8] Uotila[9] and Friedgood, Bevin and Uotila[10]). Reforzo Membrives, for example, claims not only that the pituitary glands of rats fed with thyroid fail to maintain the thyroid gland of pituitarectomized rats, but also that the thyroid glands of such rats showed an even more pronounced atrophy than those of pituitarectomized rats that had not received thyroid. In other words, the pituitary glands of rats long treated with thyroid had a depressing instead of a stimulating action on the thyroid glands of pituitarectomized rats.

The precise mode of action of TSH on the thyroid is now the subject of lively study. Collip[11] cites Eitel et al.[12] as having shown that TSH acts directly on the gland, not through an intermediary. Galli-Mainini[13] has confirmed this. Collip further cites Schneider and Widmann[14] as having demonstrated that TSH will cause symptoms of thyrotoxicosis faster than thyroxine, which suggests that it cannot be considered merely as a liberator of thyroxine. However, the explanation for this relation may be that thyroxine after administration has to be altered in its molecular structure before becoming physiologically active, and that this process requires time, whereas the thyroid when stimulated by TSH puts out its hormone in more immediately available form.

Indeed, the whole problem of the form in which hormones are secreted and act on their end-organs is important but not well understood. Chow, Greep and van Dyke[15] have treated various hormones with various enzymes and apparently have shown that when TSH is broken down enzymically below the protein level, it ceases to exert a hormonic effect. It is really unknown in what form thyroid hormone is carried in the blood and in what form it exerts its end-organ effect. It is stored in the follicle in a form which DeRobertis[16] describes as an optically homogeneous, highly viscous, refractile fluid (colloid). Its viscosity, he finds, diminishes after the injection of TSH and for a short period after the administration of potassium iodide. After a longer period on iodide, the viscosity of colloid increases. It is extremely interesting that DeRobertis was able to demonstrate in colloid obtained from single follicles a proteolytic enzyme which digests a gelatin substrate. This observation is interesting in connection with the work of Salter and Pearson,[17] which showed that thyroid proteins can be synthesized enzymically. The thyroid hormone, however, does not appear to circulate as a protein, at least not as thyroglobulin, for Lerman,[18] precipitating with thyroglobulin-immune serum, could find none in the circulating blood in hyperthyroidism, hypothyroidism or euthyroidism. It may be broken down again enzymically between thyroid cell or follicle and end-organ. Indeed, hormone physiology is rapidly entering the realm of enzyme chemistry.

TSH is also somewhat elusive when searched for in body fluids, but less so than thyroid hormone. Hertz and Oastler[19] found evidence of thyrotropic activity in the blood and urine of myxedematous patients, but not in that of thyrotoxic or normal subjects. Rawson and Starr[20] demonstrated large quantities of TSH in the urine of totally thyroidectomized patients and failed to recover it from the urine of thyrotoxic ones. In the urine of normal young men, evidence of some thyrotropic activity was obtained, but much less than in that of those who had been thyroidectomized. Bastenie[21] has also found thyrotropic activity in the urine in certain cases of myxedema. Robinson[22] studied the bloods of patients with various sorts of thyroid disease, including myxedema and thyrotoxicosis, and was unable to demonstrate a thyrotropic effect in any of them. Collard, Mills, Rundle and Sharpey-Schafer[23] also searched for TSH in the blood. In normal subjects, they could find none, even after the injection of TSH at a time when the subjects were thyrotoxic from this injection. In thyrotoxicosis, they got positive assays in 4 out of 15 cases. Positive assays were also obtained in spontaneous and postoperative myxedema and in patients with severe proptosis and ophthalmoplegia, as discussed below. Loeser[24] injected large amounts of TSH into the blood stream of rabbits and was able to detect it for only thirty minutes after injection in the intact animal, but for much longer periods in the thyroidectomized one. Seidlin,[25] in a similar study, observed TSH in the urine of thyroidectomized guinea pigs that had been injected with large amounts of TSH, but could not recover it after injection into normal guinea pigs. Observa-

tions of this character raise the question whether the thyroid gland removes TSH from the blood stream or in some way inactivates it. Rawson, Sterne and Aub[26] reported that TSH, when exposed to tissue cultures of normal rabbit thyroid, lost its physiologic activity, but that no other tissue had this property except thymus and lymphatic tissue. These investigators further found that thyrotropic activity could be restored if the medium was heated in a sealed vessel at 100°C. for one hour. About 80 per cent of the original thyrotropic activity, which had been completely lost during exposure of the medium to thyroid tissue, could be recovered in this fashion. Furthermore, it was found that thyrotropic activity can be found in heated urine when it appears to be absent before heating. These observations, undoubtedly extremely important, indicate that the thyroid gland inactivates TSH, but does not remove it from the blood stream, and that somehow or other, in this process of inactivating TSH, the thyroid parenchyma receives a stimulus which causes it to become hyperplastic and to increase its secretion of thyroid hormone. This is essentially the conclusion also of Collard and his collaborators.[23]

The morbid physiology as found in the thyrotoxicosis of Graves's disease may well be due not to an increased secretion of TSH by the pituitary, but to an increased sensitivity of the thyroid cells to TSH. The work of Stephens[27] supports such a view. He placed guinea pigs on starvation diets and observed that the thyroids of such animals became atrophic, but also that such thyroids were many times more sensitive to TSH than those of normally fed animals. These results suggest that the observations of Hertz and Means[28] and Andersen[29] — that severe weight loss, with or without thyroid therapy, sometimes precipitates thyrotoxicosis — may also be explained on the basis of hypersensitivity of the thyroid to TSH action. Friedgood, Bevin and Uotila[10] have also shown that the effect of TSH is significantly enhanced by adrenalin and by pilocarpine. They suggest that pilocarpine acts through the adrenal medulla and that adrenalin makes thyroid cells more sensitive to TSH. This brings to mind the once well-known Goetsch test.

The nature of the hormonic imbalance in various clinical syndromes has been studied by Galli-Mainini.[30] This investigator exposed normal guinea-pig thyroid to patients' serum in the Warburg apparatus and noted the effect on the oxygen absorption of the tissue (QO_2). For control, guinea-pig thyroid was exposed to normal human serum and the result was expressed as the percentage variation of the QO_2 of thyroid in patients' serum from that in normal serum. Such a procedure discloses whether the hormonic action of a patient's serum is more or less thyroid-stimulating or thyroid-depressing than is that of a healthy person. Presumably, it shows whether thyrotropic activity of the pituitary or pituitary-depressant activity of the thyroid is in the ascendency. Of course, the activity of antihormones of various sorts may enter the picture. In classic Graves's disease, Galli-Mainini found evidence of an excess, relative or absolute (presumably the latter because the basal metabolic rate is elevated), of thyroid hormone activity. By thyroidectomy this was corrected. There was an excess of thyrotropic activity in acromegaly and also in those peculiar cases of Graves's disease which Means, Hertz and Williams[31] and Means[32] have called Graves's disease with dissociation of thyrotoxicosis and ophthalmopathy, or a special ophthalmic type of Graves's disease. In untreated primary myxedema, there was an elevation in QO_2, and in treated cases, there was a slight elevation in two and reduction in two others. This separation of Graves's disease into two types is further discussed below.

With regard to the finding in acromegaly, it is of interest that Davis[33] found the thyroid enlarged in 50 per cent of a series of 166 cases of acromegaly, and for contrast with this, we may recall that it has been known since 1851 that the pituitary is hyperplastic in cretinism (Nièpce[34]) and since 1889 that it shows changes after thyroidectomy (Rogowitsch[35]). In other words, in acromegaly, the enlarged pituitary may stimulate the thyroid; in hyperthyroidism, the lack of thyroid secretion may stimulate the pituitary.

There are other humoral agents than TSH which affect the function of the thyroid. Iodine is, of course, the time-honored one. The endocrine function of iodine has been made the subject of exhaustive critical review in two recent monographs (Elmer[36] and Salter[4]), to which the reader is enthusiastically referred. That iodine inhibits or counteracts the thyrotoxicosis induced by TSH administration, much as it does the spontaneous thyrotoxicosis of Graves's disease, is well established. Salter points out that such action may be either directly on the thyroid, on the anterior pituitary and its TSH, or on end organs peripherally. Salter and Lerman[37] have discussed the first of these as a mass action due to increased iodine concentration, which favors the storage of thyroid protein. Some writers, notably Marine,[38] believe that thyroid function is totally dependent on the pituitary, but the work of Chapman[39, 40] indicates that the thyroid can respond with increase in parenchymal-cell height to iodine lack in pituitarectomized animals, and Vanderlaan, Vanderlaan and Logan,[41] studying the QO_2 of animals to which

TSH was given with and without iodine, reached the conclusion that iodine acts directly to inhibit the metabolic activity of the thyroid. On the other hand, Chapman has found a physiologic action of iodine in animals without thyroids. This appeared in experiments in which it was shown that although the level of iodine intake does not affect the growth curves of intact animals, there was less weight loss in thyroidectomized animals on high iodine intakes than in those on low. Chapman suggested the possibility of the production of a thyroxinelike material in the tissues. In any event, it seems likely that the action of iodine on the pituitary-thyroid axis may be on more than one front.

As has become increasingly apparent recently, other chemical agents than iodine may exert a seemingly specific effect on the thyroid, or on the pituitary-thyroid axis. Since the work of Hunt[42] in 1905 and of Chesney, Clawson and Webster[43] in 1928, it has been known that cyanides and vegetables containing these may be goitrogenic. Rawson, Hertz and Means[44] reported the case of a man who, after a year's treatment with potassium sulfocyanate for hypertension, rapidly developed the following weird syndrome: hyperplastic goiter with loud bruit, hypothyroidism, exophthalmos and blood iodine at the myxedema level. His thyroid promptly reverted to normal size, and his hypothyroidism disappeared merely on omission of sulfocyanate. The biopsy showed a wildly hyperplastic thyroid — hyperplastic but impotent, because his general state showed that he was suffering from a shortage of thyroid hormone. Kobacker[45] has reported a similar case, in which the picture went to that of full-blown myxedema. Kobacker's patient recovered on omission of sulfocyanate and exhibition of thyroid, but a year later, when sulfocyanate was resumed, the myxedema recurred. Dr. Herrman L. Blumgart tells me that a similar case has been observed at the Beth Israel Hospital, Boston, and from the Mayo Clinic (Fahlund[46]) comes the report of a patient who developed what appeared to be acute thyroiditis as a result of sulfocyanate therapy for hypertension.

At the same time that these human cases in which sulfocyanates had had a significant effect on the thyroid gland were being studied, experimental work was appearing indicating that the sulfonamide drugs and other sulfur-containing substances may also cause thyroid hyperplasia (MacKenzie and MacKenzie,[47] Astwood[48] and Richter and Clisby[49]). Thus, not only do cyanides and cyanates appear to be goitrogenic, but also a group of substances containing sulfur. The role of sulfur in the economy of the thyroid gland becomes interesting. One point of difference between cyanide or cyanate thyroid hyperplasia and that caused by the sulfonamides is that the former is preventable by the administration of iodine while the latter is not preventable by this means.

How these agents work on the thyroid gland is of great interest but not settled. Do they act through TSH, directly on thyroid cells, or on the end organs of the thyroid hormone? The last-mentioned theory has been widely held but at the present writing seems unlikely. A group of New Zealanders has done significant work on this question (Kennedy and Purves,[50] Griesbach[51] and Griesbach, Kennedy and Purves[52]). These investigators caused goiter in rats by feeding seeds of the Brassica (cabbage) family of plants. The goitrogenic agent is presumably a cyanide of some sort. It was found that these seeds were highly goitrogenic, producing a clearly hyperplastic type of thyroid gland in intact animals, but had no such effect in hypophysectomized rats. Also, thyroid hyperplasia caused by feeding of the Brassica seed regressed after hypophysectomy, despite the continued administration of the seed. From these results, the authors concluded that the active principle of Brassica seeds cannot stimulate the thyroid gland directly, but requires the mediation of the thyrotropic hormone. They were also able to show that certain changes occur in the anterior pituitary glands of Brassica-fed rats — namely, a rapid increase in basophilic cells and a simultaneous loss of acidophilic cells. They concluded that the basophilic cells are the source of TSH. Sharpless and Hopson[53] had previously found quite similar changes in soybean-fed rats. Iodine or desiccated thyroid increased the proportion of acidophils and decreased the proportion of basophils, but only thyroid produced the normal percentage of basophils.

Whether any practical application to treatment will arise from these experiences with cyanides, cyanates, sulfonamides and so forth, it is impossible to say at present. In any event, it is worth the physician's while to know that sulfocyanate administration can cause goiter and hypothyroidism and that thyroid or iodine will prevent or control it; and also it can be said that the information is of great scientific interest, and may provide a new approach to the study of the pituitary-thyroid axis, or of the relation between the thyroid gland and its end organs, the cells of the body.

The relation between vitamins and thyroid and other endocrine activity is being given considerable attention. Carrière, Morel and Gineste[54] have studied the effect of both excess and deficiency of various vitamins on the thyroid gland in guinea pigs. An excess of either vitamin A or C was

found to inhibit the gland, an excess of vitamin B to stimulate and an excess of vitamin D still further to stimulate. It was concluded that vitamins A and C may be helpful in hyperthyroidism, but that vitamin D and heliotherapy are contraindicated. The action of vitamin B in these experiments is of academic interest only because there is abundant evidence that this vitamin is helpful in the treatment of thyrotoxicosis (Means, Hertz and Lerman,[55] Frazier, Brown and Vars[56] and Bickel[57]). Wohl and Feldman[58] suggest that hyperthyroidism destroys and depletes vitamin A reserves in the body. This is evidenced by pathologic dark adaption in 18 out of 20 patients with thyrotoxicosis. Azerad[59] also gathered evidence of the same sort and concluded that vitamin A may be useful in thyrotoxicosis.

Thyroid-gonad interrelations also awake some interest. Nathanson, Brues and Rawson[60] found that testosterone propionate is capable of stimulating the thyroid and parathyroid glands of the intact immature female rat. It is not clear whether this is a direct effect or one routed through the pituitary gland; the latter was thought more likely.

Estrogenic substances have been tried in the treatment of thyrotoxicosis, with, on the whole, conflicting results. Robinson[61] treated 5 patients with primary Graves's disease and 2 with toxic adenoma with massive doses of Progynon B, without success except in a menopausal case in which the relation of the result to therapy given was uncertain. Goldman, Goldman and Kurzrok,[62] on the other hand, treated 8 women with hyperthyroidism with large doses of Progynon B. Five of these patients were at the menopause, and all showed improvement. These authors conclude that some cases of menopausal thyrotoxicosis respond favorably to treatment with estrogenic hormone.

In the radioactive iodine approach to thyroid physiology and therapeutics, progress continues to be made. After studying the uptake of iodine by the thyroid gland under a variety of experimental and clinical conditions, Hertz and Roberts[63] have recently made use of radioactive iodine in the treatment of thyrotoxicosis, with some encouraging results. Hamilton and Lawrence[64] have also reported results in 3 cases. Since the original paper on the use of radio-active iodine in the study of thyroid physiology by Hertz, Roberts and Evans,[65] a considerable literature has accumulated. Hamilton, Soley and Eichorn[66] have introduced the autoradiogram, by which they show, as would be expected, that hyperplastic thyroid tissue has the greatest ability to concentrate iodine. Perlman, Chaikoff and Morton[67] have studied iodine uptake by various tissues and find that thyroid tissue retains over a hundred times as much as others. This is a confirmation of the observations by Hertz, Roberts, Means and Evans.[68] The authors conclude that the thyroid gland retains iodine selectively, whereas its escape from other tissues is by diffusion only. They also showed that thyroxine is rapidly formed in the thyroid glands of both rats and sheep, but that a larger portion of administered iodine is found in the form of diiodotyrosin than thyroxine. Leblond and Sue[69] have found that TSH augments the power of the thyroid gland to fix iodine. The ensemble of their results, they conclude, on animals hypophysectomized or treated with TSH shows that this hormone controls the metabolism of iodine in the thyroid. In view of the work of Chapman,[39, 40] this statement may need some revision. In a later study, Mann, Leblond and Warren[70] gathered evidence which indicates that iodine does not exist as such in the noniodized gland of the dog. Inorganic iodine does not appear to be the major source of the iodine of diiodotyrosin. Therefore, the conversion of radioactive iodine into diiodotyrosin must take place at the cell membrane unless it arises elsewhere in the body and is secondarily fixed as such in the thyroid cells — a possibility that the authors consider unlikely. Diiodotyrosin appears to be the natural precursor of thyroxine. The radioactive iodine approach has even been applied to comparative physiology, Gorbman and Creaser[71] having shown that iodine is specifically localized in the endostyle of lamprey larvae. This organ, therefore, must be a primordial thyroid gland.

The methods of determining the iodine levels of the blood have been improved to the point of great clinical usefulness. The information to be got is analogous to that yielded by the basal metabolic rates. Salter, Bassett and Sappington,[72] for example, studying the relation of clinical symptoms, basal metabolic rate and blood iodine, found that in 71 cases in which the clinical impression of thyroid status — that is, hyperthyroid, euthyroid or hypothyroid — and the basal metabolic rate were in agreement, there was also a high degree of agreement between basal metabolic rate and the protein-bound iodine in the blood. In the 29 cases in which there was no such agreement, the blood iodine gave a better agreement with the clinical impression, and the authors therefore regard it as a better yardstick of thyroid function than the basal metabolic rate. It is, however, harder to do and more costly. Bassett, Coons and Salter,[73] studying the naturally occurring iodine fractions of the blood and their clinical behavior, divided these into T iodine (thyroxinelike), D iodine (diiodotyrosin-like), P iodine (protein bound) and

I iodine (inorganic). The ratio, T:P, gave the following results in different states of thyroid function: myxedema, 0.19; normal, 0.73; and hyperthyroidism, 0.76, 0.71 and 0.76. Thus, except in myxedema, in which little or no thyroxine circulates in the blood, the P fraction "appears to be a practical and useful method for clinical investigation and routine diagnosis, because it affords at least a roughly quantitative measurement of the circulating thyroid hormone."

The special ophthalmologic problems of Graves's disease hinted at in my previous report[1] have aroused much interest in the intervening years. Indeed, one might almost say that a new specialty of endocrinologic ophthalmology is a-borning, and rightly so, for neither the endocrinologists nor the ophthalmologists seem to know much about this peculiar field. However, it is untrue to suggest that the subject is a new one. Marine[38] states that the experimental study of exophthalmos began as early as 1858 with the work of Müller,[74] and Gley,[75] in 1910, reported that animals could develop exophthalmos following thyroidectomy. In discussion of Gley's paper, Poncet[76] remarked that the mechanism in Basedow's (Graves's) disease seems to result from a dysthyroidism amounting to a more or less severe poisoning. If then Gley had removed the entire thyroid-parathyroid apparatus, suggested Poncet, why might not there have been a vicarious exophthalmos-producing action exerted by some other organ, perhaps the pituitary? Gley did not appear to value Poncet's suggestion very highly, but it looks at present as though Poncet had made a very prophetic remark, and that Gley had missed the significance of his own observations.

The pathogenesis of exophthalmos has been studied both experimentally and clinically by many investigators, and it can be taken as well established, as shown in 1932 by Loeb and Friedman[77] and in 1933 by Marine and Rosen,[78] that exophthalmos can be produced by the administration of anterior pituitary, and also that thyroidectomy enhances such action. Marine[79] further claims that both the adrenal glands and the gonads are involved in the endocrine hook-up. Certainly, it appears that progressive exophthalmos is more easily produced experimentally in males, and although Graves's disease is more common in women, progressive or malignant exophthalmos is relatively more frequent in men. Other reports of experimental production of exophthalmos with anterior pituitary are numerous (Friedgood,[80] Smelser,[81] Paulson[82] and Aird[83]). Also well established now is the fact that in human Graves's disease, exophthalmos may become aggravated and may take on a progressive course following thyroidectomy. Among recent papers on this subject are those of Daniels,[84] del Castillo and Reforzo Membrives,[85] Jensen,[86] Means Hertz and Williams[31] and Soley.[87]

The pathology of progressive exophthalmos in Graves's disease seems to be established as one chiefly of swelling of the orbital muscles, with lymphoid infiltration, but also edema of the entire contents of the orbit (Dudgeon and Urquhart,[88] Moore,[89] Naffziger,[90] Duthie[91] and Smelser[92]). The sequence of events in its development has been reconstructed by Galli-Mainini.[93]

From the practical side, the important point is that there are certain patients with Graves's disease in whom thyroidectomy is contraindicated. They are to be recognized (Means, Hertz and Williams[31] and Means[32]) by the fact that their eye complaints and signs are more striking than their thyrotoxic ones, and that they make a superstandard response to iodine, often to minus levels of basal metabolic rate. Their thyrotoxicosis is usually easily handled by iodine alone, and when this is not sufficient, x-ray treatment to the thyroid may be used. For the eye condition, in which hyperfunction of the anterior pituitary — relative if not absolute — is probably a factor, thyroid may be given (on the theory that it depresses the pituitary), either alone or in combination with iodine. Haines[94] states that iodine and thyroid together have been used at the Mayo Clinic in cases of Graves's disease with severe ophthalmopathy and a low basal metabolic rate since 1922. Results are variable, but the treatment is worth trying; when it is insufficient, irradiation of the orbits or of the pituitary gland may be tried.

The use of thyroid for any purpose in the treatment of Graves's disease demands explanation. In addition to the indication mentioned above, Rienhoff[95] has used it for a different purpose, namely, to cause atrophy or prevent regeneration of the fragment left behind after subtotal thyroidectomy. For this purpose, he gives thyroid preoperatively to thyrotoxic patients and finds that no aggravation of symptoms results. In passing, we may note that Silex,[96] in 1896, claimed to have cured a case of Basedow's (Graves's) disease with thyroid tablets! Related to these observations of Rienhoff's, in that it also represents a suppression of thyroid activity by the administration of thyroid hormone, is the work of Farquharson and Squires,[97] in which it is shown that long-continued exhibition of thyroid to patients with so-called "nonmyxedematous hypometabolism" causes a depression in thyroid gland activity manifested by the fall of the basal metabolic rate on the omission of thyroid, to a lower level than the original one. The thyroid glands of these patients became indolent under the continued artificial supply of thyroid hormone, or perhaps their pituitary glands became indolent

and no longer stimulated their thyroid glands. Of course, the development of an antithyroid hormone during thyroid administration is another possible but, I believe, unlikely explanation of these results.

The question of liver involvement in thyrotoxicosis is always an important one. Haines, Magath and Power[98] find that the excretion of hippuric acid is reduced in a significant number of cases, an indication that the liver is often functionally disturbed. McIver and Winter[99] have shown experimentally that the administration of thyroxine increases the vulnerability of the liver to chloroform but, somewhat surprisingly, that this is not a result of glycogen depletion.

Of the treatment of Graves's disease in general, it is interesting that in the Thyroid Clinic of the Massachusetts General Hospital we have come full circle in a quarter century.[100] In the years 1919-1922, half the cases were treated by nonsurgical methods. In 1932-1935, surgery was employed in 95 per cent. In 1942, half surgical, half nonsurgical procedures are being employed. The nonsurgical cases include the special ophthalmopathic type in which we believe thyroidectomy contraindicated, and a variety of others treated successfully by iodine alone, radioactive iodine or x-ray.

In the field of myxedema, I should like to stress particularly the importance of distinguishing between the primary thyroid form and the pituitary form with secondary hypothyroidism (Castleman and Hertz,[101] Means, Hertz and Lerman[102] and Lerman and Stebbins[103]). The practical reason is that the indications for treatment are different. Thyroid alone totally relieves the former; it is not alone sufficient in the latter, but must be supplemented by other endocrine agents and salt. The salt is used as a preventive to adrenocortical insufficiency, which may be induced by thyroid alone. Thompson and his co-workers[104] have shown that the administration of TSH has no effect in human myxedema. This is what one would expect. They[105] have also shown quantitatively the relative ineffectiveness of thyroxine by mouth. Talbot et al.[106] have demonstrated that the level of serum phosphatase of infants and children with untreated hypothyroidism is abnormally low. It is restored to normal by adequate thyroid therapy. The phosphatase level can be used as a measure of thyroid deficiency.

Angina pectoris, which appears in myxedema on treatment with thyroid, is well known and is one of the complications to guard against in the inauguration of substitution therapy. Mussio Fournier and Fischer[107] have shown that another type occurs while the patient is myxedematous and disappears on thyroid therapy.

What may be called a positively charming piece of research on hypothyroidism has been done by Richter,[108] who placed rats in cages and supplied them with rolls of paper from which they could tear off bits to make nests. The amount used in nest building was measured and found very constant: thyroidectomized rats used much more paper than normal ones. Recall the human being with myxedema who requires much more bedclothing!

Of malignant disease of the thyroid, space permits me to say nothing. Perhaps, after all, this is not a thyroid but a cancer problem.

Of curiosities in the thyroid field, I may mention the report of an echinococcus cyst of the thyroid by Blum, Boquet and Hantcheff[109] and one of hemochromatosis of the thyroid gland by Graham and Mallory.[110]

In the field of surgery of the thyroid, there appears to be nothing radically new. The surgeon's point of view is well stated in a recent study by Albright and Clute.[111] It differs, of necessity, somewhat from that of the physician because the surgeon thinks in terms of operations, whereas the physician thinks in terms of patients. Certain patients will doubtless have to have portions of their thyroid glands removed for many years to come. Occasionally, they may require total thyroidectomy, and when such procedures are necessary, a high surgical skill is available. But removal is not always the best way to bring about restoration to health in the person with a diseased thyroid, nor are the results of removal always perfect. I shall close this report with the prophecy that surgery will be used less and less in this field as the endocrinology becomes better understood.

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CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

ANTE-MORTEM AND POST-MORTEM RECORDS AS USED IN WEEKLY CLINICOPATHOLOGICAL EXERCISES

FOUNDED BY RICHARD C. CABOT

TRACY B. MALLORY, M.D., *Editor*

CASE 28421

PRESENTATION OF CASE

A sixty-nine-year-old physician was admitted because of severe chest pain.

Three years previously, the patient, who was known to have had hypertension for at least ten years, had suffered with occasional attacks of dyspnea accompanied by a feeling of faintness, which required admission to a hospital. After enforced rest, he recovered and was able to get about, enjoying only limited activity. However, in spite of this limitation of activity, he noticed occasional attacks of substernal oppression, particularly on exertion. During the next two years he again entered a hospital twice for brief periods of study and rest. He carried on very little practice during this time. Three months previously, the attacks of substernal discomfort became more severe and occurred more frequently, and two months later, he entered a community hospital. While there, he had more and more trouble of this same sort, even while resting in bed. During the fourth week of his hospital stay, after a good night and soon after waking, he was seized with a very severe anterior chest pain radiating down both arms, down his back and into both legs with great intensity. The leg pain was said to have been similar to that of sciatica. This attack continued more than twelve hours in spite of the repeated administration of Dilaudid.

Physical examination showed a well-developed, obese man who was obviously acutely ill. He was slightly cyanotic and dyspneic. Breathing was irregular and of Cheyne–Stokes type. The examination of the heart revealed the maximum apical impulse 12 cm. to the left of the midsternal line in the sixth intercostal space. The retromanubrial dullness was not increased. The heart sounds were of mediocre quality. The rhythm was regular. The pulmonic second sound was sharp. No murmurs were audible. There was some increased filling of the neck veins. The radial pulse was thready, and the vessel wall was soft; no pulse deficit was noted. The lungs were normal. The abdomen was distended. No masses were felt, and no tenderness of the liver edge could be elicited. There was a slight amount of pitting edema over both ankles. No pulse was felt in the vessels of the feet or in the groin. There was no clubbing of the fingers or toes.

The blood pressure was 150 systolic, 115 diastolic. A slight alternation of the pulse was noted when the blood-pressure cuff was at this systolic pressure. The pulse rate was 110.

An electrocardiogram was said to have shown sinoauricular tachycardia. The cardiac rate was 120. The PR interval was 0.25 second. The T waves were low in Leads 1, 2 and 3 and of fair amplitude in Lead 4.

The patient did poorly, continued with the same picture of pain, shortness of breath and cyanosis and died four days later, in spite of supportive therapy in the form of oxygen and sedatives.

DIFFERENTIAL DIAGNOSIS

DR. FRANCIS R. DIEUAIDE: Although the recorded examination of the heart is not entirely clear so far as its size is concerned, I take it to mean enlargement, probably downward and outward, of moderate degree. The PR interval in the electrocardiogram was considerably more than it should have been. At the same time, there was no bradycardia, but a tachycardia. The patient was obese and was known to have had hypertension. These are general data of some importance.

To proceed at once to the final major episode, among the things one might consider is a large arterial embolus. That is suggested especially by the absence of pulsation in the feet and groin and perhaps might have fitted in with the attack of severe pain. But it seems very unlikely in this case. It offers no explanation of the preceding attack of pain or of the previous history of the patient. Furthermore there was no source for such an embolus. Large arterial emboli usually occur in cases of mitral valvular disease. This patient had no evidence of valvular disease, endocarditis or auricular fibrillation. It is true he had been in bed off and on. One might think of the possibility of his having a thrombus in a leg vein and an embolus from that, but to use that possibility one would have to suppose a "paradoxical embolus," which I cannot do.

The early story raises the question whether the patient had syphilitic aortitis. There is no report of a blood test for syphilis, which would not be decisive but which one would naturally like to have. Perhaps we might assume it had been done and was negative. There were no signs of aortic regurgitation, but we must remember, of course, that a patient may have a huge saccular aneurysm of the aorta without aortic regurgitation. There was no evidence of enlargement of the aorta on

physical examination, and we have no information about any x-ray picture of the chest. There was no physical sign of an aneurysm. On the other hand, one has to remember that an aneurysm at the back of the arch of the aorta or of the descending thoracic aorta would be extremely difficult to pick up on physical examination. Sometimes these are missed on x-ray examination. We know, in this connection, that the patient had hypertensive disease, which means that, if he had syphilitic arterial disease in addition, he had two diseases. I exclude syphilitic aortitis on the basis of the evidence that we have.

Then the question arises whether the patient had a dissecting aneurysm. It might, perhaps, be better if we had another name for that condition to separate it from saccular aneurysm, but the name seems to be fixed. The patient's age fits in satisfactorily enough. Most patients with dissecting aneurysm are between fifty and sixty, but I do not take the limits too seriously. The patient was known to have hypertension, which fits well with the diagnosis of dissecting aneurysm. The description of the major attack of pain is also compatible. We may guess that, soon after waking in the morning, the patient was not very active, so that there was no particular connection between the pain and activity, which is typical for the onset of dissection. Pain first occurred in the front of the chest and radiated down both arms. Radiation down the arms is much commoner with acute coronary occlusion than with dissecting aneurysm, but many cases of coronary occlusion have no radiation into the arms and a certain number of cases of dissecting aneurysm do have such radiation. The pain also went down the back and into both legs. I should take the radiation into the legs to be fairly strong evidence of dissection. The absence of pulsation in the groins and in the feet also fits in with dissection. We are not told the condition of the patient's legs and feet, except that they were pulseless. We do not know whether any neurologic changes or any limitation of motion existed.

Dr. Tracy B. Mallory: There were none.

Dr. Dieuaide: It is an interesting fact that a group of patients with dissecting aneurysm, as well as patients with other aneurysms of the descending aorta, have various neurologic changes in the legs, which are very important diagnostically when they are present.

If we think the patient had a dissection I suppose the question might be raised whether he also had an old dissection, because we know that there are a few patients who have an almost silent dissection with formation of a second aorta and subsequent further dissection and rupture. We have no particular reason to think that occurred in this patient, although I do not believe it is out of the question. The question might also be raised whether he is one of the few patients who have dissection with coarctation of the aorta. We have no good evidence of that. He had hypertension in his arms; we do not know the popliteal blood pressure.

Then we must, of course, consider the diagnosis that I mentioned first — coronary occlusion with myocardial infarction. The early part of the history very strongly suggests coronary sclerosis. These repeated attacks, rather severe in nature, are suggestive of coronary insufficiency. The major attack, following which the patient died, does not resemble the ordinary development of myocardial infarction. The disappearance of the pulsation in the legs has no particular relation to myocardial infarction, unless it were a later event, following embolism. The patient did not show the picture of shock following this accident, at least according to the data we have. The blood pressure was well maintained. In the case of an infarct followed shortly by death, the blood pressure usually falls markedly.

Then we come to the electrocardiogram, which is troublesome. It showed increased auriculoventricular conduction time (0.25 second). No statement is made regarding digitalis, which is an important omission.

Dr. Paul D. White: That is an error. He had been fully digitalized because of the dyspnea — for some years, as a matter of fact.

Dr. Dieuaide: He was digitalized, then, and had been regularly, so that although changes in the auriculoventricular conduction time are common in myocardial infarction, we ought to place this finding aside. It would be remarkable, however, to have increased auriculoventricular conduction time as the only electrocardiographic evidence of infarction.

Dr. White: May I correct my last statement? I find that, although he had had much digitalis in the past, he had had none within the last week or two. So there was not enough digitalis in his system to produce the delay in auriculoventricular conduction.

Dr. Dieuaide: That makes this finding more important. Perhaps Dr. White would like to discuss it. Since digitalization is not the explanation, we must consider the other possibilities. The patient may have had a chronically prolonged conduction time as a part of arteriosclerotic heart disease. We do not know about that because we have no previous electrocardiogram. Myocardial infarction, however, seems to be a better explana-

tion. At any rate, we cannot connect this finding with a dissecting aneurysm.

DR. WHITE: From my experience I should say the reverse, namely, that heart block, either auriculoventricular or intraventricular (bundle branch), is much more often evidence of chronic coronary heart disease than of an acute process. In most persons, heart block is discovered either accidentally by electrocardiograms or as a result of symptoms of faintness and not following a typical episode of acute myocardial infarction, whereas the great majority of patients who have perfectly classic attacks of acute myocardial infarction have no heart block at all or only for a few days, in the rare cases of posterior wall infarction. There are exceptions, but that is the rule.

DR. DIEUAIDE: Do you favor infarction rather than dissection here?

DR. WHITE: I should say that coronary heart disease, but not acute infarction, was one of the conditions present. The changes in the ST segments and T waves are more important than the presence of block with respect to an acute episode.

DR. DIEUAIDE: Concerning the rest of the electrocardiogram, the fact that the T waves were low in normal leads and not in Lead 4 gives us no help.

DR. WHITE: This record was taken about six hours after the attack.

DR. DIEUAIDE: In summary, my interpretation of the case is that the patient, who had hypertension, probably did have coronary sclerosis and that he suffered from chronic impairment of his myocardial reserve. I interpret the major accident to be a dissection of the thoracic aorta that extended down into the abdominal aorta.

DR. MALLORY: Would you like to speculate on the mechanism by which the dissection might have caused death.

DR. DIEUAIDE: You raise the question because of the long interval?

DR. MALLORY: Yes, in part. Dissection per se is not a lethal condition. Patients have had dissection sometimes with and sometimes without symptoms and have lived many years afterward.

DR. DIEUAIDE: I do not think I can offer a good explanation for it.

DR. WHITE: May I ask Dr. Dieuaide if he thinks a likely explanation of death might have been the final rupture of the adventitia of the aorta, with hemorrhage into one of the serous cavities.

DR. DIEUAIDE: Accepting the diagnosis, I should think that would be a natural end, but we have no data that describe what the termination was like.

DR. WHITE: It was sudden.

DR. MALLORY: The blood pressure strikes me as unusual—a very high diastolic pressure and an extremely low pulse pressure.

DR. WHITE: In both coronary occlusion and dissection of the aorta, I have seen high blood pressure maintained. I have noted hypertension in some cases only during coronary thrombosis, doubtless as the result of pain; thus the response of different individuals varies greatly. In this case, the maintenance of high blood pressure favors dissection of the aorta rather than myocardial infarct, as you have intimated.

CLINICAL DIAGNOSES

Hypertensive and coronary heart disease.
Dissecting aortic aneurysm.
Angina pectoris.
Congestive failure.

DR. DIEUAIDE'S DIAGNOSES

Dissecting aneurysm of thoracic and abdominal aorta.
Hypertension.
Coronary sclerosis.
Myocardial infarction, old.

ANATOMICAL DIAGNOSES

Dissecting aneurysm of aorta and great vessels of neck.
Cardiac tamponade.
Arteriosclerosis: coronary, moderate, and aortic, marked.
Infarcts of kidneys, partial and complete.

PATHOLOGICAL DISCUSSION

DR. MALLORY: This man did have a dissection of the aorta. We found a tear in the intima about 2 cm. above the aortic valve. From that point, dissection had occurred backward to the annularis of the aortic valve and forward almost down to the iliac arteries. One rather unusual feature of the case was that there was an extensive dissection of the carotid and innominate arteries. It is not uncommon for dissection to pass the bifurcation of the aorta and to extend several centimeters down the iliacs. There was little involvement of the iliacs here, whereas in contrast the dissection of the vessels of the neck was very marked. I think it is conceivable that, with a little closer observation, some symptoms might have been made out to indicate that, but there is nothing in the record.

The terminal episode was rupture of the outer layer of the aorta into the pericardium, with death from cardiac tamponade. The heart was markedly hypertrophied, weighing 800 grams. The coronary arteries showed moderate atheroma

and some degree of narrowing, although not severe, and no points of occlusion or any fresh thrombi were noted. There were some peculiar changes in the kidneys—some localized areas of both complete and incomplete infarction. There is a difference in susceptibility to anoxemia between the glomeruli and the tubules, and at a certain critical level, one may see infarction of the tubules in the presence of normal glomeruli. That was the case here.

DR. WHITE: At the time of my examination of the patient, there was no objective indication that aortic dissection had occurred, except for the absence of arterial pulsations in the legs, which was, to be sure, important. There was no evidence of impaired circulation to the head or arms. I looked for that. Mentally he was very clear. The reference of pain to the arms was perhaps the only indication of this spread. He had angina pectoris decubitus without a high degree of coronary occlusion. Associated with the heart size, I suppose the two important points about the diagnosis are the pain, which had characteristically radiated down into the legs, and the fact that the electrocardiogram fitted aortic dissection much more than it did acute coronary occlusion. In acute infarction of six hours' duration and with intense pain still going on, there should be considerable change in the ST segments or T waves of the electrocardiogram; the long PR interval was a red herring, which could mean a chronic lesion of the bundle of His without its being important.

CASE 28422

PRESENTATION OF CASE

A thirty-four-year-old woman was referred to the hospital because of chest pain.

The patient had been in good health and had been active until about one month prior to admission, when she developed an upper respiratory infection with coryza, slight transient sore throats and malaise. Two or three days afterward, late one afternoon, she suddenly experienced a severe sharp, steady, nonradiating pain in the anterior chest just to the right of the sternum at the level of the fourth rib. The pain was aggravated by coughing and respirations, by lying down on the right side and by downward traction on the right arm. The pain persisted, with sharp exacerbations on coughing, for one week, during which time the patient remained in bed. She was afebrile, and there were no sputum, night sweats, hemoptysis, dyspnea, palpitation and orthopnea at that time. On the third day after the onset, her physician made a diagnosis of pleurisy and accordingly strapped the chest, with some relief. Soon after this, she resumed ambulatory activities, but had several more attacks of the same pain, milder in degree and lasting approximately one hour. Because of the persistent pain, an x-ray film of the chest was taken two weeks before entry. This showed "congestion of the right lung." Since the x-ray study, the patient had had no further pain or other symptoms. She had taken no cognizance of her weight variations, but her clothes remained well fitted.

The family history and past history were noncontributory, except that she had occasionally noted ankle swelling in the evening.

Physical examination revealed a well-developed and well-nourished woman in no acute distress. Examination of the heart and lungs was negative. There was slight tenderness on pressure over the spine at the level of the sixth dorsal vertebra. The abdominal examination was not remarkable.

The blood pressure was 130 systolic, 80 diastolic. The temperature was 99.8°F., the pulse 80, and the respirations 20.

The examination of the blood revealed a red-cell count of 4,770,000 with a hemoglobin of 90 per cent, and a white-cell count of 10,100 with 74 per cent polymorphonuclears. The urine examination was negative, as was the blood Hinton test.

An x-ray film of the chest demonstrated an 8-by-5-by-6.5-cm., slightly lobulated, homogeneous mass in the right cardiophrenic angle (Fig. 1). Its anterior surface touched the anterior chest wall, and its lower pole reached to the diaphragm. No calcium was seen within it. The heart and lungs were not remarkable. The diaphragm was normal in position. An x-ray film of the dorsal spine showed no evidence of disease.

Fluoroscopy confirmed the findings of a lobulated tumor in the anterior mediastinum. The fifth day after admission, the patient was operated on.

DIFFERENTIAL DIAGNOSIS

DR. JACOB LERMAN: Perhaps we had better look at the x-ray films first.

DR. GEORGE W. HOLMES: The shadow that you see in the left lung is not important. Here is the shadow under consideration. Two oblique and a lateral view were taken. I should place the lesion in the anterior mediastinum. The shadow is quite homogeneous, sharply defined and lobulated. That is, it appears to be a solid tumor. So far as we can tell, it is in contact with the anterior chest wall.

DR. LERMAN: Could it be encapsulated fluid?

DR. HOLMES: No, because of the location. We practically never see fluid in that area. The heart and lungs are apparently normal.

DR. LERMAN: The differential diagnosis here centers about the types of mediastinal tumors. I shall first discuss lesions arising outside the mediastinum that eventually lodge in the mediastinum, and second, lesions arising in the mediastinum itself.

One should consider diaphragmatic hernia. Only a very unusual one lodges in the right chest. One might suppose that the hernia went through the anterior attachment of the diaphragm. This type, however, is extremely rare, and I mention it only in passing.

Intrathoracic goiter has to be considered, but it must be of an extremely unusual type to fit this case. Intrathoracic goiters in this region are rare; most occur in the upper mediastinum. Certainly the shape of this tumor is unusual for intrathoracic goiter. Usually, it is a single round nodule and not a lobulated mass that plunges down into the chest to rest on the diaphragm, and it lodges posteriorly rather than anteriorly.

I do not believe this is an aneurysm, because no definite connection between the mass and the aorta was visualized. The presence of pulsations is not mentioned, although they are not absolutely necessary for diagnosis. Moreover, there is no history or physical findings of syphilis, and the Hinton test was negative. I am not at all concerned about aneurysm.

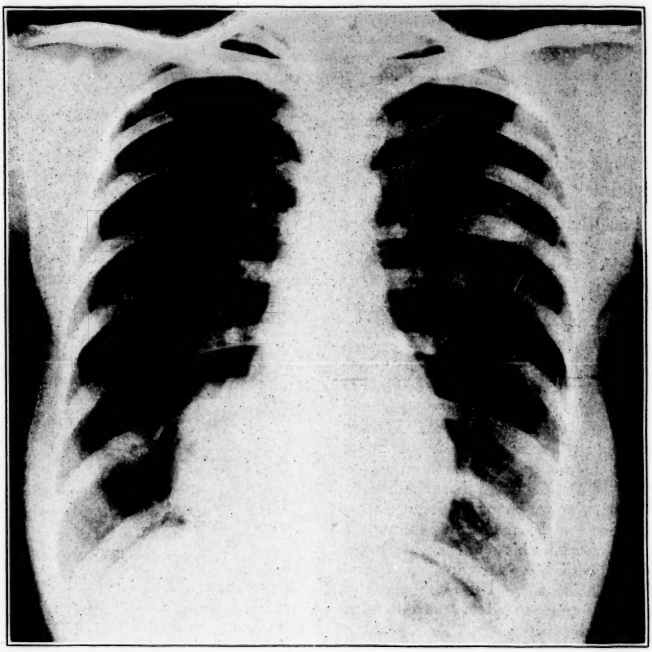

FIGURE 1.

In considering the diagnosis of mediastinal tumor, one must first settle the question whether the mass is benign or malignant. I think we can state definitely that this mass is not a malignant tumor. The patient was symptomless, except for inconstant pain; there was no evidence of invasion of surrounding structures and organs, and there was no toxemia. Consequently, we can rule out a malignant type of tumor.

Although I doubt that I can make a better diagnosis than just benign mediastinal tumor, I must consider the several varieties. The description of

the tumor, the short duration of pain and the unknown duration of the tumor are consistent with dermoid, which also is the commonest statistically. On the other hand, several cases with similar findings that have been discussed at these meetings were found to have had either a neurofibroma, chondroma, lipoma or cyst. We saw one mediastinal tumor here a year ago that gave similar symptoms and had a similar appearance in the x-ray films, which the pathologist called hemangioma. One should mention thymoma as a possibility. It must have extended from its origin in the thymus down to this region. I have no way of confirming this diagnosis.

As Dr. Holmes said, it is unusual to find encapsulated fluid in this location, although the history of pleurisy a month before admission raises the question of fluid in the pleural space. Moreover, lobulation of the mass argues strongly against encapsulated fluid. Consequently, I shall not consider it further.

In conclusion, I believe this is a benign mediastinal tumor, either neurofibroma or dermoid.

Dr. William B. Breed: I wonder if enough stress has been laid on the fact that this whole episode was ushered in by an acute respiratory infection. That may be of some importance, and the mass may still be encapsulated pus. Perhaps this point should be stressed just a little more than it was in the discussion.

Dr. Lerman: Dr. Churchill has emphasized many times that the symptoms of these patients have no relation to the mediastinal tumor. I have been influenced by his opinion. Many patients come in with bizarre complaints, and a tumor is found incidentally. I think the onset of the respiratory infection served to focus attention on something in the chest.

Dr. Ralph Adams: Did this mass move with swallowing?

Dr. Tracy B. Mallory: I do not believe so.

Dr. Edward D. Churchill: This is all a guessing game, for it is very difficult to arrive at any preoperative diagnosis except mediastinal tumor, benign or malignant. There are two or three additional diagnoses that occurred to me as I listened to the discussion. I should think of a hernia through one of the apertures of the diaphragm and should have advised a barium enema. There is another lesion that we have come to recognize particularly along the right border of the pericardium,—namely, a thin-walled cyst containing clear fluid. These cysts are comparable to the cystic hygromas that are found in the neck. Perhaps Dr. Mallory can say whether they are of lymphatic origin or of endothelial origin from adjacent serous cavities.

I wish Dr. Holmes would take a stand on the question whether this particular patient should have received a diagnostic dosage of radiation therapy to rule out lymphoma or another radiosensitive tumor before operation.

Dr. Holmes: As a general rule, I think the diagnosis should be established, whenever possible, before we subject a patient to x-ray therapy. But it depends largely on the severity of the operative procedure planned. If it is to be a simple operation, probably x-ray therapy should not be given; on the other hand, if it is a dangerous operation, I should advise giving a small dose.

Dr. Churchill: Will you feel badly if some day I enucleate such a tumor and it turns out to be lymphosarcoma or lymphoma?

Dr. Holmes: No.

Dr. Churchill: Will you, Dr. Mallory?

Dr. Mallory: No. It might be good treatment. I think when an isolated tumor is resectable it is wise to remove it, because very long cures often follow the procedure.

Clinical Diagnosis

Mediastinal tumor (? dermoid cyst, ? neurofibroma, ? lymphoblastoma).

Dr. Lerman's Diagnosis

Benign mediastinal tumor (neurofibroma or dermoid).

Anatomical Diagnosis

Pleuropericardial cyst.

Pathological Discussion

Dr. Mallory: This patient did turn out to have a cyst filled with perfectly clear fluid. The cyst has a fibrous wall with an occasional smooth muscle fiber in it, looking essentially like pleura. It is lined with a low cuboidal epithelium that occasionally seems multilayered, which is probably due to tangential sectioning; it seems likely that the epithelium lining was only a single layer thick. So far as the appearance of the cells is concerned, they could either be mesothelial, such as those that line the pleura, or endothelial, which one would find lining a lymphatic vessel. I do not believe I can answer Dr. Churchill's question. I have a little preference for the theory that this sac is made up of pleural or pericardial tissue than that it represents a cystic lymphangiomatous tumor, such as a cystic hygroma of the neck.

Dr. Holmes: Perhaps we should have observed it on inspiration and expiration to see if there was a change in shape, which one might expect if it had a thin wall and contained fluid.

DR. MALLORY: Should this tumor perhaps have been needled before operation?

DR. CHURCHILL: I do not think so.

DR. MALLORY: If it had been, could you have made the diagnosis?

DR. CHURCHILL: Probably, but we should not have known what to do in the way of treatment. I do not believe it is without danger to put a needle in so close to the pericardium. There is always a possibility that one is dealing with an aneurysm of the auricle.

Dermoids are likely to be a bit higher on the right and a little closer to the lung root. When a tumor lies in the cardiophrenic angle, a simple cyst must be seriously considered.

DR. MALLORY: Sometimes, there is a rather unusually large amount of fat tissue in that location. Does that ever cause clinical confusion in a case of this sort?

DR. CHURCHILL: I do not recall having been misled by a fat pad.

DR. ALLEN G. BRAILEY: The patient would have been perfectly well if left alone?

DR. CHURCHILL: I think she would have.

DR. MALLORY: We have no idea of the rate with which these cysts grow. It is quite doubtful that this had anything to do with the symptoms.

DR. CHURCHILL: I also think that it is very doubtful. One must remember, however, that the presence of an x-ray shadow of this type is sufficient reason for employment rejection by many large industrial plants and, of course, by the armed forces. She can now join the WAACs or WAVES.

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AN ELOQUENT SERMON

The number of physicians on extended active duty and the figures on the 1942 quotas, as of September 1, are now available from the Procurement and Assignment Service. The latter furnish interesting and disturbing data, particularly concerning some of the New England states. The state providing the lowest percentage of its quota of physicians for 1942 is Nevada, which has obtained but 56 per cent. The second lowest is Illinois, in which the figure is 63 per cent. The next two lowest are Connecticut and New York, each having supplied but 64 per cent of their quotas. For Massachusetts, the figure is 67 per cent; for New Hampshire, 79 per cent; for Vermont, 82 per cent; for Rhode Island, 84 per cent; and for Maine, 99 per cent.

For a community spoken of as the "Cradle of Liberty," Massachusetts hardly shows to advantage in this picture when compared with such states as New Mexico with 205 per cent of its total quota, Louisiana, with 196 per cent, Alabama, with 179 per cent, South Carolina, with 160 per cent, Kentucky, with 159 per cent, and North Carolina, with 151 per cent. Twenty-six states in the Union have supplied above 100 per cent of their quotas. When one realizes that Massachusetts stands fifth from the bottom, only four other states, Nevada, Illinois, Connecticut and New York, having lower percentages, then it can be said that these figures preach an eloquent sermon.

A SEMICENTENNIAL

It is occasionally valuable to stop in the course of one's daily rounds and survey the activities of one's fellow workers. The opportunity usually arises in relation to an anniversary, a birthday or the completion of a long period of service. Such an event will be celebrated on Friday, October 23, at the Boston Medical Library, for on that date Mr. James F. Ballard, the director, will have completed a service of fifty years as a valued employee of that institution.

Beginning in 1892, as a boy helping in the stacks, Mr. Ballard has worked his way up to the directorship of the library and has made a name for himself in the front rank of medical librarians. This position has been recognized by his election to the presidency of the Medical Library Association and to other offices. He is widely known for his classification of medical books, which is used in almost every medical library in this country. In the past, he has been consulted by the Rockefeller Foundation and its General Education Board for advice in establishing medical libraries in this country and abroad. There are few men living who know more about medical books and their accession, classification and care. His knowledge of medical periodicals, moreover, is extensive.

It should be pointed out that, in addition to his work as a medical librarian, he has been for many years a substantial citizen of the Town of Milton, has sent three of his children through college and has two sons now serving in the armed forces.

This creditable career is largely the result of his own efforts, for his preliminary schooling was scant and knowledge came to him largely through continued application and long hours of hard work. His nights, Sundays and holidays, which for many people are times of relaxation, have been freely and almost continuously given to the Boston Medical Library. Rarely would one not find him at work in the evening or on Sunday afternoon, particularly during the last twenty-five years, when he has had executive responsibility.

It is of interest, moreover, that he chose as his hobby one of the most difficult branches of medical literature, namely, incunabula or books printed in the fifteenth century. Here he had to acquire a working knowledge of Latin and a deep appreciation of these books and their significance, as well as a considerable technical knowledge regarding their classification, for the printer, place of publication and author are often unknown. There are, in addition, many details to be learned about the type used, the paper, the dating of the publication and the relation of the printed book to the same material in manuscript form circulated before the discovery of printing. All these have been Mr. Ballard's particular interest in the last two decades, and the library has turned to him for a new catalogue of its renaissance and medieval manuscripts and its incunabula, which is now in the course of publication.

Few individuals have the opportunity of serving one organization for half a century. It is even rarer to have the service so genuine and efficient as that given by Mr. Ballard to the Boston Medical Library. The *Journal* therefore takes great pleasure in extending to him heartiest congratulations on this semicentennial anniversary and wishes him good health in the future so that he may continue his work, the thing nearest his heart.

MEDICAL EPONYM

Rovsing's Sign

Dr. Thorkild Rovsing (1862-1927), director of the Surgical Clinic at the University in Copenhagen, described "Indirektes Hervorrufen des typischen Schmerzes an McBurney's Punkt [Indirect Elicitation of Typical Pain over McBurney's Point]," in the *Zentralblatt für Chirurgie* (34: 1257-1259, 1907). Being unable satisfactorily to examine in the usual way two patients whom he suspected of having appendicitis, he was able to bring out the typical pain by this maneuver. A portion of the translation follows:

> Both patients showed such unusual sensitiveness to palpation that a careful examination of the region of McBurney's point seemed not only impossible but inadvisable. It occurred to me that the typical pain might possibly be elicited by pressure on the descending colon, in the *left* iliac fossa. I laid my left hand flat on the abdomen and with the right hand forced its fingers down against the colon, compressing it. The hand was then allowed to glide upward toward the sigmoid flexure.

R. W. B.

MASSACHUSETTS MEDICAL SOCIETY

ANALYSIS OF CAUSES OF MATERNAL DEATH IN MASSACHUSETTS DURING 1941

The five-year study of the maternal mortality in Massachusetts, conducted by the Section of Obstetrics and Gynecology, ended with the deaths occurring during the year 1941. Two hundred and forty-seven deaths were listed by the Massachusetts Department of Public Health for investigation, and of these, 5 were found, after investigation, to have no relation to pregnancy. Although these are included in the tabulation of the causes of maternal deaths (Table 1), the cases will not be reviewed. An example of such a case is as follows:

> Following the death of this patient, autopsy proved that pregnancy did not exist. The patient died of septicemia, peritonitis and parametrial abscess. One pregnancy preceded this fatality by eleven months, but there was no subsequent history of abortion, nor did the autopsy reveal any uterine change characteristic of pregnancy.

The death rate, 2.9 per 1000 living births, was practically identical with that for 1940, which was 2.8 per cent. Although that is a creditable figure,

an analysis of the deaths will clearly show how this can be lowered.

It must be borne in mind that the allocation of deaths was left entirely to the discretion of the investigator. An attempt was made to place each

TABLE 1. *Causes of Maternal Deaths.*

CAUSE	NO. OF DEATHS
Sepsis, including abortions	48
Medical (pneumonia, cardiac disease, chronic nephritis and so forth)	42
Embolism	39
Hemorrhage, including separated placenta and placenta previa	31
Albuminuria and eclampsia, including toxemia	27
Surgical	10
Anesthesia	10
Ectopic pregnancy	6
Ruptured uterus	5
Transfusion	4
Suicide	2
Inverted uterus	2
Cerebral hemorrhage	2
Pernicious vomiting	2
Cause unknown	2
Shock	2
Abdominal pregnancy	1
Aneurysm	1
Chemical	1
Hydatidiform mole	1
Psychosis	1
Sudden death	1
Anaphylaxis	1
Cancer of breast	1
Nonpuerperal	5
Total	247

case in which there was a possibility of more than one classification in the group that indicated the primary cause of death. This is illustrated by the following case:

> Autopsy showed that the patient had rheumatic heart disease, pulmonary infarction and cerebral embolism. The patient died almost four weeks after delivery. The case was classed under "cardiac disease," because there was, in addition, a definite history of heart disease of many years' standing.

It is, in one sense, distinctly unfair to include cases of suicide in computing the maternal death rate. Pregnancy may have been a contributing factor in the mental unbalance associated with such fatalities, but the cases in no way represent obstetrical mismanagement. Furthermore, the case of aneurysm, although interesting in itself, was not a true maternal death.

Beginning with next week's issue of the *Journal*, the 48 cases of sepsis will be reviewed; and in subsequent issues, cases under the various other headings will be analyzed.

DEATH

HANDY — HARRY T. HANDY, M.D., of Scituate, died October 8. He was in his sixty-ninth year.

Born in Marion, Dr. Handy received his degree from Harvard Medical School in 1897. He was a fellow of the Massachusetts Medical Society and the American Medical Association.

He is survived by his widow, a brother and a sister.

MISCELLANY

NOTES

Eleven appointments to the teaching and research staff at the Harvard Medical School, effective during the present academic year, were recently announced as follows: assistant in ophthalmology, Fred S. Thorne, of Newtonville, M.D. Harvard '18; assistant in medicine, Jack D. Cohen, of Brookline, M.D. Tufts '37; assistant in pediatrics, Edward L. Pratt, of Boston, M.D. Harvard '40; assistant in surgery, Arnold Starr, of Newton, M.D. Tufts '28; research fellow in anatomy, David L. Bassett, of Stanford University, California, M.D. Stanford '39; research fellow in medicine, Marshall Clinton, Jr., of Cambridge, M.D. Buffalo '40; research fellow in surgery, Mercier Fauteux, of Westmount, Quebec, Canada, F.R.C.S. (C) Royal Canadian College of Surgery '31; Austin Teaching Fellow in Physiology, Aristides A. P. Leao, of Rio de Janeiro, Brazil, M.A. Harvard '42; instructor in surgery, David D. Berlin, of Brookline, M.D. Tufts '23; assistant in bacteriology and immunology, Morris J. Pickett, of Boston, Ph.D. Stanford '42; research fellow in comparative pathology and tropical medicine, Henry D. Hoberman, of Bridgeport, Connecticut, Ph.D. Columbia '42. The appointments of Drs. Pickett and Hoberman are also effective in the Harvard School of Public Health.

CORRESPONDENCE

RELATION OF PERIPHERAL DISEASES TO PULMONARY FIBROSIS

To the Editor: In the past eighteen months, there have appeared in the *Journal* three papers of much greater significance than the implication of their titles. In the April 17, 1941, issue, Linenthal and Talkov reported three cases of pulmonary fibrosis in Raynaud's disease, and in the September 17, 1942, issue, they reported two additional cases, whereas in the September 18, 1941, issue, Banks had a paper entitled, "Is there a Common Denominator in Scleroderma, Dermatomyositis, Disseminated Lupus Erythematosus, the Libman–Sacks Syndrome and Polyarteritis Nodosa?" In the six cases reported by these three authors, Raynaud's disease, scleroderma and arthritic conditions were associated with pulmonary fibrosis.

Ten years ago, I reported before the Boston Society of Psychiatry and Neurology a group of cases in which these conditions and Dupuytren's contracture were associated with pulmonary fibrosis and other pulmonary conditions, and in the October, 1934, issue of the *Journal of Nervous and Mental Disease*, I reported twenty-nine cases in which Raynaud's disease, scleroderma, Dupuytren's contracture, noninfectious arthritis and other peripheral conditions were associated with fibrosis and other pulmonary conditions, no prior description of this syndrome having been found in the literature.

Banks, Linenthal and Talkov, without having read this paper and, I believe, without obligation to any other authors, have now reported six cases exhibiting this syndrome, including complete laboratory data and almost complete pathological data. I say "almost complete pathological data" because I believe that, when one of the conditions in this syndrome appears clinically, the others are present subclinically and may be found by the pathologist.

If this ten-year-old concept, that pulmonary fibrosis, Raynaud's disease, noninfectious arthritis, Dupuytren's

contracture, sclerodema and some other conditions are not clinical entities but parts of a syndrome, is once accepted, then progress in the study of every one of these conditions should be accelerated.

HALE POWERS, M.D.

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BOOK REVIEWS

The 1941 Year Book of Industrial and Orthopedic Surgery. Edited by Charles F. Painter, M.D. 12°, cloth, 432 pp., with 353 illustrations. Chicago: The Year Book Publishers, Incorporated, 1941. $3.00.

Dr. Painter is to be congratulated on the clear and concise manner in which he has summarized the contributions to orthopedic surgery that have been published during the past year. Each article has a new idea and a different approach to treatment. A larger section has been written on industrial medicine in an attempt to keep pace with this important branch of medical practice. There are numerous excellent illustrations. The selection and arrangement of the material are good. Although no two persons compiling a year book on orthopedic surgery would make identical selections of articles, there are few who would criticize the selections Dr. Painter has made. This little book should be on the reading list of all industrial and orthopedic surgeons.

Rabies. By Leslie T. Webster, M.D. 8°, cloth, 168 pp., with 8 illustrations and 22 tables. New York: The Macmillan Company, 1942. $1.75.

In much of the literature on rabies, the lines between scientific fact and speculation have not been clearly drawn, and many of the articles are not easily accessible. This book is a compilation of existing literature and attempts to furnish sound data to those who would otherwise have difficulty in obtaining it. The first part of the book discusses the diagnosis of the disease, and the second covers its prevention, citing controversial results. It is stated, contrary to popular opinion, that "there is no definite evidence that vaccine treatment, following exposure to rabies, confers any striking protection against the disease" and that "investigations of the efficacy of vaccine treatment should be continued from all angles." The author states emphatically, however, that "persons exposed to rabies should be given vaccine treatment with confidence that then there is small likelihood of development of the disease."

This book should be of great value to physicians, veterinarians, public-health officials and research workers but, because of its technical nature, is not suitable for laymen.

The 1941 Year Book of Pathology and Immunology. Pathology. Edited by Howard T. Karsner, M.D. *Immunology.* Edited by Sanford B. Hooker, M.D. 12°, cloth, 623 pp., with 136 illustrations. Chicago: The Year Book Publishers, 1941. $3.00.

This book gives well-selected reviews of the developments in pathology and immunology during 1941. However, comparing the abstracted articles with such a complete list as that given in the *Index Medicus*, one finds that it deals almost entirely with papers in English, owing to abnormal wartime conditions, which limit the availability of almost all scientific journals issued abroad.

The twelve chapters on pathology, edited by the experienced and dynamic director of the Institute of Pathology of Western Reserve University, take up 349 pages and review general pathology and the pathology of tumors, of the cardiovascular, hematopoietic, respiratory, urinary and nervous systems, of the alimentary tract, of the male and female genitalia, of the organs of locomotion and of the glands of internal secretion. In this section, there are 129 illustrations, all reproduced from the articles abstracted; most of them are photographs showing histologic features of lesions, which are of great value to the reader. Among the large amount of information yielded by hundreds of analyses that are presented to the reader, the following are of particular interest: a review prepared at the invitation of the editor by Virgil A. Moon on the pathologic changes underlying the development of shock; a summary given by Eben J. Carey of his contributions to knowledge of the function of striated muscles; an abstract of studies on the bicuspidal semilunar valves, furnished by Simon Koletsky; an interesting review prepared by Aldo Luisada on favism; and data from Page on the new aspects of the nature of chemical changes occurring in arteriosclerosis. The interpretation of the analyses is helped by timely observations from the editor. A few papers, such as the one of Esmond R. Long entitled "Constitution and Related Factors in Resistance to Tuberculosis" and three others, dealing respectively with transmission of susceptibility to cancer, the identity of "inhibitor" and "antibody" in virus-induced rabbit papillomas and the union in vitro of the papilloma virus and its antibody, are included in the section covering the pathology of tumors, although their subjects, being of immunologic nature, ought to be included in the section on immunity to tumors.

The second part starts with a tribute to Hans Zinsser by his successor, J. Howard Mueller. Zinsser, who served Harvard, Columbia and Stanford universities as bacteriologist and immunologist for more than thirty-five years, had been properly regarded, for more than a quarter of a century throughout the world, as the academic personification of immunology applied to the study of infectious diseases. The chief attraction in this part of the book is found in the chapter on blood groups, where the recent advances in blood transfusion, inaugurated by Landsteiner's and Wiener's discovery of the Rh factor and its relation to erythroblastosis foetalis, are authoritatively discussed by Wiener himself and by Philip Levine. The contributions in the various fields of immunity are divided into chapters dealing with immunity to bacterial diseases, immunity to viral diseases, immunity to diseases due to protozoa, fungi and higher parasites, immunity to tumors, chemotherapy, anaphylaxis and allergy, blood groups, immunochemistry, bacteriology and bacterial nutrition, and technics and miscellaneous topics. In the first chapter, the influence of war is reflected in the prevalence of papers dealing with tetanus, although the flow of publications on immunity concerning diphtheria and pneumococcal infections and so forth is not lowered. In the chapter on viral infections, in which an introductory article by Thomas M. Rivers gives a résumé of current developments in this field and the growing importance of vaccines for prevention, the recent research work on bacteriophage, encephalomyelitis, choriomeningitis, poliomyelitis and so forth is ably reviewed; however, owing to the war and to the interest in Horsfall's vaccine, papers dealing with influenzal virus prevail. The chapter on the immunology of para-

sitic diseases supplies additional information to that included in Culbertson's book on immunity against animal parasites. Immunity to tumors supplements the section on their pathology edited by Karsner; whereas the chapter on chemotherapy merely supplements the subject, which is more extensively reviewed in other volumes of the series, its inclusion being justified by a sort of synergism between chemotherapeutic agents and antibodies in pneumonia and by the remarkable contributions supplied to this field of gramicidin and tyrothricin, the bactericidal fractions prepared from René J. Dubos's aerobic, sporulating soil bacillus. Those especially interested in the fields of anaphylaxis, allergy and immunochemistry in the realm of antigens and antibodies will find these sections particularly instructive on account of the critical remarks and suggestions, which are presented as a comment of the editor to some of the papers reviewed. A few illustrations and a table showing the clinically important cutaneous tests, which have been taken from an article of Charles A. Janeway, also give useful information and witness the ability of the editor to convey knowledge to the reader. When details on the methods used are essential, as in Landsteiner's and Di Somma's sensitization of animals with simple chemical compounds or in Heidelberger's quantitative chemical studies on complement, the editor reproduces them thoroughly from the original articles. An up-to-date report on the developing egg as a culture medium heads the reviews on bacterial nutrition, and a description of the electron microscope begins the last chapter, which is devoted to technics and miscellaneous topics.

A comprehensive index to subjects and authors, covering both pathology and immunology, supplies a valuable guide to this book.

Biological Symposia: A series of volumes devoted to current symposia in the field of biology. Edited by Jaques Cattell. Vol. V. *Comparative biochemistry: intermediate metabolism of fats: carbohydrate metabolism: biochemistry of choline.* Edited by Howard B. Lewis, Ph.D. 8°, cloth, 247 pp., with 31 tables, 20 figures and 2 plates. Lancaster, Pennsylvania: The Jaques Cattell Press, 1941. $3.00.

This is the latest of a series in biology published by the Jaques Cattell Press, and comprises the four symposiums arranged by the Council of the American Society of Biological Chemists for the April, 1941, meeting of the Federation of American Societies for Experimental Biology. It is thus well planned and authoritative. The contributors include such eminent investigators as Samuel Soskin, H. E. Longenecker, C. F. Cori, Otto Meyerhof and Vincent du Vigneaud. There are fifteen papers in all. Each is limited to ten to fifteen pages, which makes assimilation of the subject matter easy.

The first symposium, on comparative biochemistry, seeks to show some of the phases of modern biochemistry as they apply to plants and to animals and birds. An interesting question raised in plant biochemistry is the significance of the alkaloids, which may represent unexcretable end products of the plant's nitrogen metabolism. The importance of niacin (nicotinic acid), choline and the betaines in plants, as well as in man, is discussed. In a paper on end products of nitrogen metabolism in animals, a comparative study is made of mechanisms of conjugation of nitrogenous products, and of variations in uric acid and purine metabolism. A third paper, on the merging of growth factors and vitamins, points out that choline is an essential growth factor for the pneumococcus, and nicotinic acid for *Staphylococcus aureus.*

In the symposium on the intermediate metabolism of fats, Soskin and Levine state that ketone bodies are not formed because of faulty carbohydrate oxidation, but occur normally and independently of such oxidation. The peripheral tissues of the diabetic patient dispose of ketone bodies as fast as those of the normal person, and when ketone bodies appear in excess, it is due only to accelerated production of these substances in the liver. Thus the "ketogenic-antiketogenic ratios," as formerly used, are meaningless.

One of the most interesting papers in the book is that of Longenecker on the formation of animal body fat. It has recently been shown, by "tagging" molecules with deuterium in place of hydrogen atoms, that the depot fat, instead of being laid down only in periods of excess food intake, is constantly in a state of flux, although its amount may not change. The conversion of fat to carbohydrate has also been traced by the use of deuterium. It was shown experimentally by Longenecker that protein can be converted to fat in the animal body. In these conversions between carbohydrate, protein and fat, certain members of the vitamin B complex are essential.

The symposium on carbohydrate metabolism comprises four papers, all dealing with enzyme reactions: the oxidation catalysts, including the flavoproteins and cytochromes; the process of aerobic phosphorylation of glycogen, by which the energy from oxidations is made available to the cell for its use; the "oxidoreductions," or anaerobic molecular rearrangements; and the oxidation of pyruvic acid by the "citric acid cycle," essential in intermediate carbohydrate metabolism.

The fourth symposium, on the biochemistry of choline, is of great interest. Choline has recently been shown to prevent or cure fatty livers in depancreatized dogs or in rats fed a high-fat diet. This property of choline is known as its "lipotropic effect." Choline deficiency in the diet causes an acute hemorrhagic degeneration in the kidneys of rats. In the body, choline stimulates the formation of phospholipids, permits the productions of acetylcholine and, most significant, supplies "labile" methyl groups that the body cannot synthesize but must have for numerous methylations. One paper discusses the enzyme, cholinesterase, which destroys acetylcholine. In the final paper, du Vigneaud discusses the interrelations between choline and other methylated compounds. He and his co-workers, by the use of deuterium in methyl groups, were able to show that choline is definitely an essential dietary factor and that its methyl groups are concerned with methionine and sulfur metabolism, with creatine metabolism and with fat metabolism.

Altogether, this most stimulating collection of papers is highly recommended.

Psychosurgery: Intelligence, emotion and social behavior following prefrontal lobotomy for mental disorders. By Walter Freeman, M.D., Ph.D., and James W. Watts, M.D. With special psychometric and personality profile studies by Thelma Hunt, M.D., Ph.D. 4°, cloth, 337 pp., with 81 illustrations. Springfield, Illinois: Charles C Thomas, 1942. $4.00.

Since 1900, there have been three important new approaches toward solving the problem of mental disease. The first is psychoanalysis, which has brought many new ideas to medicine, especially regarding emotional patterns. The second is shock therapy, employing insulin, Metrazol and other chemical and physical means of altering or influencing the course of mental disease. The third

and newest of these methods involves operation on the brain itself — prefrontal lobotomy.

This new book, the first of its kind, describes the intelligence, emotions and social behavior of patients who have undergone prefrontal lobotomy for mental disorders. The work has been carefully planned and executed and leaves little to be desired in terms of complete and conscientious reporting. The surgeon will find the book interesting, just as he might have found Dr. Cushing's book on meningiomas of interest; in fact, the general outline of case study employed by Cushing has been followed by the authors. The psychiatrist will find the reports valuable in view of the alterations in personality following operation.

This is an unusual book in that it combines three important kinds of observation in one document. It includes the clinical history, with emphasis on the mental disorder, and gives a detailed account of the surgical procedure that was followed and of the follow-up reports, which are interesting and unique. In some cases, neuropathologic reports were available, and in the more successful cases detailed psychometric studies were utilized to measure the changes and improvement shown by the patient.

The authors have been very modest in reporting their results. They are keenly aware of the limitations and the experimental aspects of their studies. At the same time, they report enough substantial data to support interesting and encouraging conclusions. Until now, physicians have had to ask, Does cutting into the brain improve insanity? The answer contained in this book is, In some cases, improvement from certain psychiatric disorders has followed prefrontal lobotomy. The book is quite technical, but each physician should read it for himself to obtain his own impression. There are a few minor defects, which can be discounted in view of the great historical importance of the book.

Many neurosurgeons at present are extremely conservative in their approach to mental disorder. This book clearly indicates the type of patient for whom the operation may be suitable, and it describes with adequate clarity the technic and general management of the case.

In some quarters, the entire process of operating on the brain for mental disorder has been frowned on, since it has been regarded as too dangerous and too radical. From a study of the cases in this book, however, one gains the impression that the actual operation is not so radical as it sounds.

The book will probably do much to focus the attention of neurosurgeons and general surgeons on this problem and to stimulate their interest in the subject and their criticism of the method.

From Cretin to Genius. By Serge Voronoff. 8°, cloth, 281 pp. New York: Alliance Book Corporation, 1941. $2.75.

The author analyzes, in a philosophical vein, genius, the soul, the mind, the creative process and similar topics. He uses a wealth of observations on poets, writers, composers, artists and scientists, with considerable historical accuracy. When he comes to theorize about his material, however, he falls far short of scientific standards. He concludes, for example, "that the conscious ego occupies the superficial layer of the brain, and the subconscious the lower layers." It is from these "lower layers" that come "the profoundest thoughts of philosophers, the loftiest flights of poets, the proudest creations of artists, the noblest discoveries and inventions of scientists." Again, when discussing the electroencephalogram, he writes: "Scanning the chart, we can tell whether the thought was joyous or sad, whether the feeling experienced was happy or painful. For the electric waves change according to the character of each thought and each feeling." These are far cries from the known physiologic facts, and based on such premises, the author's arguments are highly speculative and often unwarranted.

Preeclamptic and Eclamptic Toxemia of Pregnancy. By Lewis Dexter, M.D., and the late Soma Weiss, M.D. In collaboration with Florence W. Haynes, Herbert S. Sise and James V. Warren. 8°, cloth, 415 pp., with 47 illustrations. Boston: Little, Brown and Company, 1941. $5.00.

This monograph approaches the subject from the standpoint of the internist and the research worker, rather than from that of the obstetrician. The obstetric point of view, however, is not lost sight of, since the practical application of the research carried out is stressed throughout the book. The purpose of the monograph, as stated by the authors, is twofold: to describe their experiences and interpret their findings, and to analyze the literature in the light of their studies. A timely, well-sifted bibliography is appended at the end of each chapter, making important references readily available.

Consideration is given to the nature and significance of generalized edema in normal pregnancy and in toxemia of pregnancy. The authors believe that the etiology of generalized edema cannot be explained by the well-recognized mechanical causes of edema formation, including hydrostatic pressure in the capillaries, increased capillary permeability to protein and hypoproteinemia. Nor do they regard it as due to cardiac failure, anemia, vitamin B_1 deficiency, myxedema or excessive ingestion of sodium salts. By exclusion, they suspect a primary, humoral etiology. The relation of the pressor fraction of the posterior pituitary gland to the hypertension of toxemia of pregnancy is fully discussed. Under the conditions of their experiments, Pitressin did not produce permanent hypertension when administered in both large and small repeated doses. No significant histologic changes were observed in the animals under the experimental conditions employed. So far as could be determined by the methods of extraction now in use, the pressor substance, renin, is not concentrated in the placentas of women with hypertension during pregnancy. A chapter is devoted to the arterial blood pressures of newborn babies of normal and hypertensive mothers; no significant difference in the blood pressures was found to exist. Hormones have not induced a syndrome strictly comparable to human toxemia in animals, nor does toxemia occur in them spontaneously. From their studies, the writers postulate that the improvement in blood pressure, albuminuria and edema that occurs promptly in toxemic patients following delivery is due to the removal of the placenta rather than to the removal of the fetus or to the relief of pressure on neighboring structures by the enlarged uterus.

One hundred and fifty-nine pages are devoted to the pre-eclamptic and eclamptic toxemias of pregnancy (arterial hypertension in pregnancy and the hypertensive toxemia of pregnancy). Eighty cases showing hypertension previous to the pregnancy studies were exhaustively investigated. The illustrations of the pathologic processes studied are clear and well chosen. An interesting diagram representing the factors involved in toxemia and post-toxemia is presented. Two types of hypertension in pregnancy have been differentiated — the prepregnant hypertension, uninfluenced by pregnancy, and hypertensive toxemia of preg-

nancy, which may occur in patients with or without pre-pregnant hypertension.

The chapter on treatment starts with the earlier methods, and considers all advances made in the management of this disorder. The authors advise a middle course, stressing individualization of the patient. Methods that have been found valuable are summarized under "Present-Day Treatment." Diekmann's and Irving's treatments are completely outlined and cover what is accepted as satisfactory management. Prenatal care is emphasized as an essential part of the care of these patients.

The text is interesting to read, and the illustrations are excellent. This monograph will benefit not only the student of the toxemias of pregnancy and the research worker but also the general practitioner and the clinical obstetrician.

Immunology. By Noble P. Sherwood, Ph.D., M.D. Second edition. 8°, cloth, 639 pp., with 27 illustrations and 7 color plates. St. Louis: The C. V. Mosby Company, 1941. $6.50.

This is the second edition of an introductory textbook intended for the use of medical students and others interested in immunology and serology. It contains much that should interest the clinician.

It is clearly and simply written. The author is careful to define terms that may be unfamiliar to some of his readers. The material has been rearranged so that it may be outlined more readily, and two new chapters, one on the reticuloendothelial system and the other on serum reactions, have been added. A brief introduction to colloid chemistry has been retained. Most of the references, which are unusually numerous and well chosen, have been brought up to date. The index is adequate, typographical and grammatical errors are few, and the diagrams and illustrations, several in color, are helpful.

The author tends to cite in detail the conclusions of individual research workers, which sometimes leads to unnecessary duplication. At the ends of many chapters, however, he presents well-integrated summaries and his own interpretations of the often conflicting experimental data. The historical aspects of the various subjects are briefly but adequately covered. The chapters on antigens, antibodies and specificity as applied to the laboratory diagnosis of the common infectious diseases, although a little more up to date than they were in the first edition, are not so authoritatively covered as they are in certain other texts. The chapters on complement fixation and other serologic technics, however, are especially well done.

Directory of Medical Specialists Certified by American Boards, 1942. 8°, cloth, 2495 pp. New York: published for the Advisory Board for Medical Specialists by Columbia University Press, 1942. $7.00.

This second edition of the *Directory of Medical Specialists* contains over 18,000 names of doctors certified by the fifteen American boards. Since the publication of the first edition in 1939, over four thousand physicians have successfully taken board examinations, and their names are to be found in the new edition. New information, especially concerning the graduate and postgraduate education of the diplomates, has been added. The directory has been increased in size by over nine hundred pages. Three new boards, on anesthesiology, plastic surgery and neurologic surgery, have been established since 1939, and their membership is included in the directory.

The indexing is seriously defective, since it omits the page on which the entry to the individual person is made. This omission causes unnecessary delay when one desires information on a particular person. One must first look for the name in the index, where the address and certifying board are found. This is a poor beginning, for it is necessary to look in succession for the special board, the state and the city or town, which are arranged alphabetically. All this searching would be obviated if the index noted the page in the volume where the name is listed. It is hoped that the editors will make this change in the next edition.

The work is extremely bulky, but is of inestimable value as a book of reference.

Diseases of the Nervous System, Described for Practitioners and Students. By F. M. R. Walshe, O.B.E., M.D., D.Sc., F.R.C.P. (Lond.), D.Sc. (hon.). Second edition. 8°, cloth, 35 pp., with 32 illustrations. Baltimore: The Williams and Wilkins Company, 1941. $4.50.

The fact that a second edition of this book was called for within two years is a tribute to its worth. The volume is a kind of personal report from a distinguished British neurologist, giving a summary of his experiences in a difficult field of medicine. Because of the outstanding position held by the author and his ability to write clearly and comprehensively, the book may safely be put in the hands of medical students and practitioners.

Readers should be warned, however, that they may find some personal reactions, especially to treatment, not widely held in this country. Such a statement as "tryparsamide is used in the post-pyrexial treatment of dementia paralytica" is correct but the drug is used extensively and favorable in other ways. Also, the statement that "the so-called Bulgarian belladonna treatment has no advantages over other measures" in the treatment of post-encephalitis Parkinsonism is too dogmatic for a controversial issue. Some drugs are referred to by their British trade names, unfamiliar to many American physicians. The Bragg–Paul type respirator is recommended, but in this country the Drinker box type is almost routinely used. With these points in mind, however, an American reader will find little difficulty in gaining a knowledge of clinical neurology from this book, which reflects the sound views of a leader in the field.

Your Teeth: Their past, present and probable future. By Peter J. Brekhus, D.D.S. With a foreword by Irvine McQuarrie, Ph.D., M.D. 8°, cloth, 255 pp., with 20 illustrations, 31 plates and 7 tables. Minneapolis: The University of Minnesota Press, 1941. $2.50.

This volume represents a compilation of facts and theories pertaining to dental health. The book is not intended as a text for the dental practitioner or student, but fills a gap as an informative source, useful to the layman as well as to the dentist.

Excellent chapters on the biologic and anthropologic factors concerning the development and loss of teeth are presented. A discussion on the causes of caries and pyorrhea, with a voluminous bibliography, is especially valuable.

A program for prevention of caries, with special reference to the care of children's teeth, is constructive and worthy of consideration in mapping out a nationwide program for the control of dental caries, which is so widespread in present civilization.

The author has approached the subject from a long experience in both clinical and scientific studies, with a broad vision of the future of dentistry and suggestions for further investigative studies.

(Notices on page x)